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(REV 11-2000)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER

TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371

GKS-101.0 (7911/83687)

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR

09/936852

INTERNATIONAL APPLICATION NO.
PCT/EP00/02410INTERNATIONAL FILING DATE
March 17, 2000PRIORITY DATE CLAIMED
March 17, 1999

TITLE OF INVENTION

NUCLEIC ACID MOLECULE COMPRISING A NUCLEIC ACID SEQUENCE CODING FOR A HAEMOCYANIN

APPLICANT(S) FOR DO/EO/US

Jurgen MARKL, Benjamin ALTENHEIN, Bernhard LIEB and Thomas STIEFEL

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (24) indicated below.
4. ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
 - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
 - b. ☒ has been communicated by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
 - a. ☒ is attached hereto.
 - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
 - a. ☒ are attached hereto (required only if not communicated by the International Bureau).
 - b. ☐ have been communicated by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☐ A copy of the International Search Report (PCT/ISA/210).

Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☒ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
20. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
21. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
22. ☒ Certificate of Mailing by Express Mail
23. ☐ Other items or information:

U.S. APPLICATION NO. IF KNOWN SEE 37 CFR <div style="font-size: 2em; font-weight: bold;">09/936852</div>		INTERNATIONAL APPLICATION NO. <div style="font-weight: bold;">PCT/EP00/02410</div>		ATTORNEY'S DOCKET NUMBER <div style="font-weight: bold;">GKS-101.0 (7911/83687)</div>	
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24. The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :	CALCULATIONS	PTO USE ONLY
<input type="checkbox"/> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO	\$1000.00	
<input checked="" type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO	\$860.00	
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO	\$710.00	
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4)	\$690.00	
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4)	\$100.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =		
		\$860.00
Surcharge of \$130.00 for furnishing the oath or declaration later than _____ months from the earliest claimed priority date (37 CFR 1.492 (e)). <input type="checkbox"/> 20 <input type="checkbox"/> 30		\$0.00
CLAIMS	NUMBER FILED	NUMBER EXTRA
Total claims	44 - 20 =	24
Independent claims	11 - 3 =	8
Multiple Dependent Claims (check if applicable). <input type="checkbox"/>		\$0.00
TOTAL OF ABOVE CALCULATIONS =		\$1,932.00
<input type="checkbox"/> Applicant claims small entity status. (See 37 CFR 1.27). The fees indicated above are reduced by 1/2.		\$0.00
SUBTOTAL =		\$1,932.00
Processing fee of \$130.00 for furnishing the English translation later than _____ months from the earliest claimed priority date (37 CFR 1.492 (f)). <input type="checkbox"/> 20 <input type="checkbox"/> 30		\$0.00
TOTAL NATIONAL FEE =		\$1,932.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). <input type="checkbox"/>		\$0.00
TOTAL FEES ENCLOSED =		\$1,932.00
		Amount to be: refunded \$
		charged \$

a. ☒ A check in the amount of \$1,932.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23-0920 A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

SIGNATURE

Shannon L. Nebolsky

NAME

41,217

REGISTRATION NUMBER

September 17, 2001

DATE

09/936852

JC12 Rec'd PCT/PTO 17 SEP 2001

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Jürgen MARKL, et al.)	
Serial No.:	Not yet assigned)	Attorney Docket:
Filing Date:	September 17, 2001)	GKS-101.0
)	7911/83687
For:	NUCLEIC ACID MOLECULE)	
	COMPRISING A NUCLEIC ACID)	
	SEQUENCE CODING FOR A)	
	HAEMOCYANIN)	
)	Group Art Unit:
Examiner:	Not yet assigned)	Not yet assigned

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

This paper is a Preliminary Amendment for the U.S. national phase filing of PCT/EP00/02410 filed herewith as a new patent application under 35 U.S.C. § 371. Please enter this Preliminary Amendment and amend the accompanying application as follows.

New §371 Application
Based on PCT/EP00/02410
Filed August 17, 2001
Markl, et al.

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IN THE ABSTRACT:

Please cancel the Abstract section that was originally
filed, entitled "Abstract" and substitute the new ABSTRACT.

- -ABSTRACT

The present invention relates to a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a fragment thereof with the immunological properties of at least one domain of haemocyanin. The invention furthermore relates to constructs which comprise the nucleic acid molecule and, where appropriate, a promoter suitable for expression control. In a preferred embodiment, the construct furthermore comprises a nucleic acid sequence which codes for an antigen. The invention moreover relates to host cells which contain these nucleic acid molecules and/or constructs. The invention furthermore relates to recombinant expression of the nucleic acid molecules and/or constructs in the host cells. The invention furthermore relates to haemocyanin, a haemocyanin domain, a fragment with the immunological properties of at least one domain of haemocyanin and haemocyanin fusion proteins, which are coded by the nucleic acid molecules and/or constructs. The invention furthermore relates to pharmaceutical compositions which comprise the nucleic acid molecules and/or haemocyanin, a haemocyanin domain, a fragment thereof or a fusion protein. The invention furthermore relates to liposomes which comprise the nucleic acid molecules and/or haemocyanin, a haemocyanin domain, a fragment

New §371 Application
Based on PCT/EP00/02410
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thereof or a fusion protein. The invention furthermore relates to antibodies which are obtainable by immunization of a test animal with haemocyanin, a haemocyanin domain, a fragment thereof or a fusion protein, and the use thereof in screening methods for the identification of tumours.--

IN THE CLAIMS

Please cancel Claims 1 through 44 and substitute new Claims 1 through 44.

REMARKS

Prosecution and consideration of the claimed subject matter in the accompanying patent application is respectfully requested.

I. The Amendments

The attached English translation of the claims as filed in the corresponding international patent application were amended to conform to standard U.S. practice. As a result, the originally-filed English translation of Claims 1 through 44 were cancelled and replaced with the substitute Claims 1 through 44.

A copy of the claims showing the amendments effected by this substitution of the claims is enclosed. The substitute

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Claims 1-44 are in the case and are before the Examiner. It is thus seen that no new matter has been presented. A complete, clean copy of the claims before the Examiner is enclosed herewith.

The Abstract and the claims were amended to conform to standard U.S. practice.

A filing fee is enclosed based on the number of independent and dependent claims in the application after entry of this Preliminary Amendment. No further fee or petition is believed to be necessary. However, should any further fee be needed, please charge our Deposit Account No. 23-0920, and deem this paper to be the required petition.

Respectfully submitted,


Shannon L. Nebolsky, Reg. No. 41,217

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CERTIFICATE OF EXPRESS MAILING

I hereby certify that this Preliminary Amendment including clean and marked-up copies of the Amendments, together with a 371 application and its papers and fee, are being deposited with the United States Postal Service as Express Mail Label No. EL706574854US, postage prepaid, in an envelope addressed to: Commissioner for Patents, Box PCT, Washington, D.C. 20231 on September 17, 2001.

Frank Jones

vertebrate leads to a non-specific activation of the immune system which to date is not very well understood. By the general activation of the immune system, it is then possible also to achieve an immune reaction to other foreign structures which have previously been tolerated. KLH is used above all as a hapten carrier in order thus to achieve the formation of antibodies against the hapten.

In addition to *Megathura crenulata*, the abalone *Haliotis tuberculata* also belongs to the Archaeogastropoda group, which is relatively old in respect of evolution. It is known that *Haliotis* also produces haemocyanin.

KLH is a mixture of two different haemocyanins, which are called KLH1 and KLH2. The subunit of KLH1 is a 390 kDa polypeptide which consists of eight globular domains called 1 a to 1 h according to their sequence in the subunit. On the other hand, KLH2 has a molecular weight of 350 kDa and according to the most recent data also contains 8 domains, called 2 a to 2 h. *In vivo* every type of subunit forms homo-oligomers, while no hetero-oligomers have been observed.

Amino-terminal, internal and carboxy-terminal domains have been obtained by limited proteolysis and crossed immunoelectrophoresis of the subunit of KLH1 and KLH2, and their amino-terminal sequences has been determined (Söhnngen et al., Eur. J. Biochem. 248 (1997), 602-614; Gebauer et al., Zoology 98(1994), 51-68). However, the resulting sequences do not allow designing of sequence-specific primers and/or probes which promise success for hybridization with genomic DNA. Although both KLH types have been known since 1991 and 1994 respectively, it has so far not been possible to clarify the primary structure.

At the DNA level, in respect of molluscs only the cDNA sequence of the haemocyanin subunit from the cephalopod *Octopus dofleini* is so far known (Miller et al., J. Mol. Biol. 278 (1998), 827-842). *Octopus dofleini* is phylogenetically very far removed from the archaeogastropods. A haemocyanin gene sequence from molluscs is so far not known at all.

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),

SEQ ID NO:10 (HtH2 domain c),
 SEQ ID NO:11 (HtH2 domain d),
 SEQ ID NO:12 (HtH2 domain e),
 SEQ ID NO:13 (HtH2 domain f),
 SEQ ID NO:14 (HtH2 domain g),
 SEQ ID NO:15 (HtH2 domain h),
 SEQ ID NO:16 (partial KLH1 domain b),
 SEQ ID NO:17 (KLH1 domain c),
 SEQ ID NO:18 (KLH1 domain d),
 SEQ ID NO:19 (partial KLH1 domain e),
 SEQ ID NO:20 (KLH2 domain b),
 SEQ ID NO:21 (KLH2 domain c),
 SEQ ID NO:22 (partial KLH2 domain d),
 SEQ ID NO:23 (KLH2 domain g),
 SEQ ID NO:24 (partial KLH2 domain h),
 SEQ ID NO:49 (HtH1 domain a' + signal peptide),
 SEQ ID NO:50 (partial HtH2 domain a),
 SEQ ID NO:51 (HtH2 domain b'),
 SEQ ID NO:52 (HtH2 domain d'),
 SEQ ID NO:53 (HtH2 domain e'),
 SEQ ID NO:54 (KLH1 domain e'),
 SEQ ID NO:55 (KLH1 domain f),
 SEQ ID NO:56 (KLH1 domain g),
 SEQ ID NO:57 (KLH2 domain b'),
 SEQ ID NO:58 (KLH2 domain c'),
 SEQ ID NO:59 (KLH2 domain d'),
 SEQ ID NO:60 (KLH1 domain e),
 SEQ ID NO:61 (KLH2 domain f),
 SEQ ID NO:62 (KLH2 domain g'),
 SEQ ID NO:80 (HtH1 domain a" + signal peptide),
 SEQ ID NO:81 (HtH1 domain b"),
 SEQ ID NO:82 (HtH1 domain c"),
 SEQ ID NO:83 (HtH1 domain d"),
 SEQ ID NO:84 (HtH1 domain e"),

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

The "immunological properties of at least one domain of haemocyanin" means the property of a polypeptide of inducing, in the same manner as at least one domain of haemocyanin, an immunological response of the recipient immunized with the polypeptide. "Immunological response" here is understood as meaning T and/or B cell responses to haemocyanin epitopes, such as, for example, an antibody production. The immunological reaction can be observed, for example, by immunization of a mammal, such as e.g. a mouse, a rat or a rabbit, with the corresponding polypeptide and comparison of the immune response to the polypeptide used for the immunization with the immune response to natural haemocyanins.

According to the invention, the term "antigen" includes both haptens and weak and potent antigens. Haptens are characterized in that they are substances of low molecular weight (less than 4,000 Da), but without being coupled to a carrier molecule are not capable of inducing an immunological reaction. Weak antigens are substances which can themselves already induce an immunological reaction and of which the potential to be able to induce an immunological reaction can be increased further by coupling with a carrier molecule at the protein and/or DNA level.

"His tag" means a sequence of at least 6 histidine amino acids which, by corresponding cloning and fusion with an expressible sequence, leads to a fusion protein which has at least 6 His residues on the NH₂ terminus and can easily be purified by complexing with an Ni²⁺ column.

"Cloning" is intended to include all cloning methods known in the prior art which could be employed here but which are not all described in detail because they belong to the obvious hand tools of the skilled person.

"Variants" of a nucleic acid sequences include additions, deletions, insertions or inversions and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin. Variants can be synthetic or natural. Allelic variants are an example of natural variants.

"Recombinant expression in a suitable host cell" is to be understood as meaning all the expression methods known in the prior art in known expression systems which could be employed here but which are not all described in detail because they belong to the obvious hand tools of the skilled person.

The nucleic acid sequence contained in the nucleic acid molecule according to the invention can be genomic DNA, cDNA or synthetic DNA, synthetic DNA sequences also being understood as meaning those which comprise modified internucleoside bonds. The nucleic acid sequences can furthermore be RNA sequences, which may be necessary e.g. for expression by means of recombinant vector systems. The nucleic acid sequences according to (b) are obtainable, for example, by using a detectably

marked probe which corresponds to one of the sequences described under (a) or a fragment, or a counter-strand thereof for screening cDNA/genomic DNA libraries from molluscs or arthropods. The mRNA on which the cDNA library is based is preferably to be obtained from mollusc tissues which express haemocyanin to a particularly high degree, such as e.g. mantle tissue from gastropods and branchial gland tissue from cephalopods.

Positive cDNA/genomic DNA clones are identified by standard methods. Cf. Maniatis et al., Molecular Cloning (1989) Cold Spring Harbor Laboratory Press.

In a preferred embodiment, the hybridization described under (b) or (d) is carried out under stringent conditions. Stringent hybridization conditions are e.g. 68°C overnight in 0.5 x SSC; 1% blocking reagent (Boehringer Mannheim); 0.1% sodium lauryl sarcosinate and subsequent washing with 2 x SSC; 0.1% SDS.

In a preferred embodiment, nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a) are provided. The nucleic acid sequences are preferably at least 80% homologous to one of the nucleic acid sequences described under (a). The nucleic acid sequences are particularly preferably at least 90 % homologous to one of the nucleic acid sequences described under (a). In particular, the nucleic acid sequences are at least 95% homologous to one of the nucleic acid sequences described under (a).

According to the invention, the term "homology" means homology at the DNA level, which can be determined by known methods, e.g. computer-assisted sequence comparisons (Basic local alignment search tool, S.F. Altschul et al., J. Mol. Biol. 215 (1990), 403-410).

The term "homology" known to the skilled person describes the degree to which two or more nucleic acid molecules are related, this being determined by the concordance between the sequences. The percentage of "homology" is obtained from the percentage of identical regions in two or more sequences, taking into account gaps or other sequence peculiarities.

Preferred methods for the determination of homology initially produce the greatest concordance between the sequences analysed. Computer programs for determination of the homology between two sequences include, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., *Nucleic Acids Research* 12 (12): 387 (1984); Genetics Computer Group University of Wisconsin, Madison, (WI)); BLASTP, BLASTN and FASTA (Altschul, S. et al., *J. Mol. Biol.* 215:403-410 (1990)). The BLASTX program can be obtained from the National Centre for Biotechnology Information (NCBI) and from other sources (BLAST Handbook, Altschul S., et al., NCB NLM NIH Bethesda MD 20894; Altschul, S., et al., *J. Mol. Biol.* 215:403-410 (1990)). The known Smith Waterman algorithm can also be used for determining homologies.

Algorithm:	Needleman and Wunsch, J. Mol. Biol 48:443-453 (1970)
Comparison matrix:	Concordance (matches) = + 10 Non-concordance (mismatch) = 0
Gap penalty:	50
Gap length penalty:	3

Further algorithms, gap opening penalties, gap extension penalties and comparison matrices by way of example, including those mentioned in the Program Handbook, Wisconsin Package, version 9, September 1997, can be used. The choice depends on the comparison to be made and furthermore on whether the comparison is to be made between sequence pairs, in which case GAP or Best Fit are preferred, or between a sequence and a comprehensive sequence databank, in which case FASTA or BLAST are preferred.

A concordance of 60% determined with the abovementioned algorithm is designated 60% homology in the context of this application. The same applies accordingly to higher degrees of homology.

In a preferred embodiment, the DNA sequence according to the invention is a combination of several of the DNA sequences described under (a) to (f), which can be obtained by fusion and optionally cloning, which are known to the skilled person. These combinations are of particular interest, since they are particularly immunogenic. Combinations which contain several or all of the domains in the sequence (a to h) which occurs naturally in the subunit are particularly preferred. Embodiments in which the nucleic acid sequences which code for the domains are coupled to one another directly in frame are particularly preferred.

Constructs which comprise the nucleic acid molecules according to the invention are furthermore provided. In a preferred embodiment, the construct according to the invention comprises a promoter which is suitable for expression, the nucleic acid sequence being under the control of the promoter. The choice of promoter depends on the expression system used for expression. Generally, constitutive promoters are preferred, but inducible promoters, such as e.g. the metallothionein promoter, are also possible.

In a further preferred embodiment, the construct furthermore comprises an antigen-coding nucleic acid sequence which is bonded directly to the haemocyanin nucleic acid according to the invention. The antigen-coding sequence can be located both 5' and 3' relative to the haemocyanin sequence or also on both ends. It either follows the haemocyanin sequence directly in the same reading frame, or is coupled to it by a nucleic acid linker, the reading frame being preserved. By fusion of the antigen-coding sequence with the haemocyanin sequence the formation of a fusion protein in which the antigen-coding sequence is bonded covalently to the haemocyanin sequence is intended. The antigen according to the invention is a medically relevant antigen, which is selected, for example, from: tumour antigens, virus antigens and antigens of bacterial or parasitic pathogens. Tumour antigens can be, for example, Rb and p53. The virus antigens preferably originate from immunologically relevant viruses, such as e.g. influenza virus, hepatitis virus and HIV. Pathogen antigens are, inter alia, those from

In another preferred embodiment, the construct furthermore comprises at least a part of a vector, in particular regulatory regions, the vector being selected from: bacteriophages, such as λ derivatives, adenoviruses, vaccinia viruses, baculoviruses, SV40 viruses and retroviruses, preferably MoMuLV (Moloney murine leukaemia virus).

A construct which additionally comprises a His tag-coding DNA sequence, which, when expressed, leads to the formation of a fusion protein with a His tag on the NH₂ terminus of the haemocyanin, facilitating purification of the protein on a nickel column by chelate formation, is furthermore preferred.

The invention furthermore provides host cells which contain the construct and which are suitable for expression of the construct. Numerous prokaryotic and eukaryotic expression systems are known in the prior art, the host cells being selected, for example, from prokaryotic cells, such as *E. coli* or *B. subtilis*, from eukaryotic cells, such as yeast cells, plant cells, insect cells and mammalian cells, e.g. CHO cells, COS cells or HeLa cells, and derivatives thereof. For example certain CHO production lines of which the glycosylation patterns are altered compared with CHO cells are known in the prior art. The haemocyanins obtained using glycosylation-deficient or glycosylation-reduced host cells possibly have additional epitopes which are otherwise not accessible to the immune system of the recipient in the case of complete glycosylation, so that haemocyanins with a reduced glycosylation under certain circumstances have an increased immunogenicity. From plant cells transformed with the construct according to the invention it is possible to produce transgenic plants or plant cell cultures which produce haemocyanin polypeptides, for example tobacco, potato, tomato, sugar beet, soya bean, coffee, pea, bean, rape, cotton, rice or maize plants or plant cell cultures.

The present invention also relates to a process for the preparation of a haemocyanin polypeptide. For this, the nucleic acid molecule according to the invention and/or the

construct is expressed in a suitable host cell and the protein is isolated from the host cell or the medium by means of conventional processes.

Numerous processes for expression of DNA sequences are known to the skilled person; compare Recombinant Gene Expression Protocols in Methods in Molecular Biology, volume 62, Humana Press Totowa New Jersey (1995). The expression can be both constitutive and inducible, inducers such as, for example, IPTG and Zn^{2+} being known to the skilled person. If a His tag has been fused on to the NH_2 terminus of the haemocyanin, the haemocyanin prepared can be purified by chelate formation on a nickel column. Processes for the purification of haemocyanin, in particular KLH, are to be found in Harris et al., Micron 26 (1995), 201-212. The haemocyanin is preferably purified by ion exchange chromatography and/or gel filtration chromatography. The procedure for these measures is known to the skilled person.

In another preferred embodiment, the haemocyanin prepared according to the invention is modified. The modifications include di-, oligo- and polymerization of the monomeric starting substance, for example by crosslinking, e.g. by means of dicyclohexylcarbodiimide or pegylation or association (self assembly). The di-, oligo- and polymers prepared in this way can be separated from one another by gel filtration. The formation of decamers, didecamers or multidecamers is intended in particular. Further modifications include side chain modifications, for example of ϵ -amino-lysine residues of the haemocyanin, or amino- or carboxy-terminal modifications. Modification of the haemocyanin by covalent bonding to an antigen is particularly preferred, it being possible for the antigen to be reacted stoichiometrically or non-stoichiometrically with the haemocyanin. The antigen is preferably selected from tumour antigens, virus antigens and pathogen antigens, as mentioned above. Further modifications include post-translational events, e.g. glycosylation or partial or complete deglycosylation of the protein.

In a preferred embodiment, the haemocyanin obtained by recombinant expression in prokaryotes or glycosylation-deficient eukaryotes is non-glycosylated. Haemocyanin which is glycosylated by recombinant expression in eukaryotes which are capable of glycosylation, such as yeast cells, plant cells, insect cells or mammalian cells, such as CHO cells or HeLa cells, is also possible according to the invention.

- SEQ ID NO:25 (HtH1 domain a + signal peptide),
SEQ ID NO:26 (HtH1 domain b),
SEQ ID NO:27 (HtH1 domain c),
SEQ ID NO:28 (HtH1 domain d),
SEQ ID NO:29 (HtH1 domain e),
SEQ ID NO:30 (HtH1 domain f),
SEQ ID NO:31 (HtH1 domain g),
SEQ ID NO:32 (HtH1 domain h),
SEQ ID NO:33 (partial HtH2 domain b),
SEQ ID NO:34 (HtH2 domain c),
SEQ ID NO:35 (HtH2 domain d),
SEQ ID NO:36 (HtH2 domain e),
SEQ ID NO:37 (HtH2 domain f),
SEQ ID NO:38 (HtH2 domain g),
SEQ ID NO:39 (HtH2 domain h),
SEQ ID NO:40 (partial KLH1 domain b),
SEQ ID NO:41 (KLH1 domain c),
SEQ ID NO:42 (partial KLH1 domain d),
SEQ ID NO:43 (partial KLH1 domain e),
SEQ ID NO:44 (KLH2 domain b),
SEQ ID NO:45 (KLH2 domain c),
SEQ ID NO:46 (partial KLH2 domain d),
SEQ ID NO:47 (KLH2 domain g),
SEQ ID NO:48 (partial KLH2 domain h),
SEQ ID NO:63 (HtH1 domain a' + signal peptide),
SEQ ID NO:64 (HtH1 domain h'),

The term "homology" known to the skilled person describes here the degree to which two or more polypeptide molecules are related, this being determined by the concordance between the sequences, concordance being understood as meaning both identical concordance and conservative amino acid exchange. The percentage of

"homology" is obtained from the percentage of regions in concordance in two or more sequences, taking into account gaps or other sequence peculiarities.

The expression "conservative amino acid exchange" relates to an exchange of an amino acid residue for another amino acid residue, where the exchange does not lead to a change in polarity or charge. An example of a conservative amino acid exchange is the exchange of a non-polar amino acid residue for another non-polar amino acid residue.

The homology of polypeptide molecules which are related to one another can be determined with the aid of known methods. As a rule, special computer programs with algorithms which take account of the particular requirements are employed. Preferred methods for the determination of homology initially produce the greatest concordance between the sequences analysed. Computer programs for determination of the homology between two sequences include, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., *Nucleic Acids Research* 12 (12): 387 (1984); Genetics Computer Group University of Wisconsin, Madison, (WI)); BLASTP, BLASTN and FASTA (Altschul, S. et al., *J. Molec. Biol* 215:403/410 (1990)). The BLAST X program can be obtained from the National Centre for Biotechnology Information (NCBI) and from other sources (BLAST Handbook, Altschul S., et al., NCB NLM NIH Bethesda MD 20894; Altschul, S., et al., *J. Mol.* 215:403/410 (1990)). The known Smith Waterman algorithm can also be used for determining homology.

Preferred parameters for the sequence comparison include the following:

Algorithm:	Needleman and Wunsch, <i>J. Mol. Biol</i> 48:443-453 (1970)
Comparison matrix:	BLOSUM 62 of Henikoff and Henikoff, <i>Proc. Natl. Acad. Sci. USA</i> 89:10915-10919 (1992)
Gap penalty:	12
Gap length penalty:	4
Similarity threshold:	0

The GAP program is also suitable for use with the above parameters. The above parameters are the standard parameters (default parameters) for amino acid sequence comparisons where gaps at the ends do not reduce the homology value. If sequences are very short

Further algorithms, gap opening penalties, gap extension penalties and comparison matrices by way of example, including those mentioned in the Programm-Handbuch, Wisconsin-Paket [Program Handbook, Wisconsin Package], version 9, September 1997, can be used. The choice depends on the comparison to be made and furthermore on whether the comparison is to be made between sequence pairs, in which case GAP or best fit are preferred, or between a sequence and a comprehensive sequence database, in which case FASTA or BLAST are preferred.

In another embodiment, the invention provides haemocyanin polypeptides which are obtainable by the recombinant preparation method or modifications thereof.

Haemocyanin 1 from *Haliotis tuberculata*, which has an apparent molecular weight of 370 kDa in SDS-PAGE under reducing conditions, is particularly preferred.

Haemocyanin 2 from *Haliotis tuberculata*, which has an apparent molecular weight of 370 kDa in SDS-PAGE under reducing conditions, is furthermore particularly preferred.

The haemocyanins are obtainable from whole haemocyanin from *Haliotis tuberculata* by the selective dissociation process described in the examples.

In particular, the invention provides the use of a nucleic acid molecule according to the invention which is bonded to an antigen-coding DNA sequence for specific immunization against this antigen. Without being bound to this theory, the immunization here is based on non-specific stimulation of the immune system by haemocyanin polypeptide epitopes and more extensive specific immunization by recognition of antigen epitopes by the immune system.

Such an immunization is particularly valuable in respect of pathogen antigens, and especially in respect of tumour antigens. The usability of the pharmaceutical composition according to the invention for treatment of tumour diseases also results from the cross-reactivity of the haemocyanin-specific antibodies with carbohydrate residues, which occur on the surface of tumours, such as e.g. the Thomsen-Friedenreich antigen, which occurs in the majority of human tumours, such as epithelial carcinomas, ovarian carcinoma, colorectal carcinoma, mammary carcinoma, bronchial carcinoma and bladder carcinoma.

The pharmaceutical compositions according to the invention can furthermore be employed for treatment of parasitic diseases, such as schistosomiasis, and for prevention of cocaine abuse.

Pharmaceutical compositions which comprise a haemocyanin polypeptide according to the invention in combination with one or more physiologically tolerated additives are provided as a further embodiment of the present invention. As already mentioned above, such a haemocyanin polypeptide can consist of a complete haemocyanin subunit, of one or more domains and of one or more fragments of such domains, provided that these fragments still have the immunological properties of at least one domain of a haemocyanin. Such a pharmaceutical composition is suitable e.g. as an antiparasitic composition, antiviral composition or antitumour composition due to either the non-specific immunostimulation, which is to be attributed solely to the haemocyanin, or due to the specific immune reaction to antigens associated with the haemocyanin. It can thus be employed e.g. for treatment of schistosomiasis, epithelial carcinomas, ovarian carcinoma, colorectal carcinoma, mammary carcinoma, bronchial carcinoma and bladder carcinomas, but is also suitable for treatment of high blood pressure. The treatment of high blood pressure is achieved by carrying out an immunization with the aid of haemocyanin- β -adrenergic receptor peptide constructs and/or fusion proteins.

In another embodiment, the pharmaceutical compositions according to the invention are used as vaccines. They can thus make a valuable contribution to the prophylaxis of diseases caused by known pathogens. This applies in particular to pharmaceutical compositions in which a haemocyanin polypeptide is coupled to a virus, virus

constituent, killed bacteria, bacteria constituents, in particular surface proteins from virus or bacteria envelopes, DNA, DNA constituents, inorganic or organic molecules, e.g. carbohydrates, peptides and/or glycoproteins.

According to another preferred embodiment, the pharmaceutical composition according to the invention is used for prevention of cocaine abuse.

Liposomes are particularly suitable for administration both of the nucleic acid molecules according to the invention and of the haemocyanin polypeptides. The present invention accordingly relates to liposomes which comprise a nucleic acid molecule according to the invention, a construct according to the invention or a haemocyanin polypeptide according to the invention.

Various methods for the preparation of liposomes which can be used for pharmaceutical purposes are known to the skilled person. The selectivity of the liposomes comprising the nucleic acid molecules or haemocyanin polypeptides according to the invention can be increased by the additional incorporation into the liposome of cell recognition molecules, which bind selectively to target cells. Receptor ligands which bind to receptors of the target cells or, especially in the case of tumours, antibodies directed against surface antigens of the particular target cells envisaged are particularly suitable for this.

The haemocyanin polypeptides according to the invention are furthermore envisaged as carrier molecules for medicaments, such as e.g. cytostatics. The increase in the molecular weight prolongs the physiological half-life of the medicaments considerably since the loss due to ultrafiltration in the kidneys is significantly reduced.

The vaccines are formulated by methods known to the skilled person; in some embodiments the additional use of adjuvants, such as e.g. Freund's adjuvant or polysaccharides, is envisaged.

The invention furthermore provides antibodies which react specifically with the haemocyanin polypeptide according to the invention and are obtainable by immunization of a test animal with a haemocyanin polypeptide. Polyclonal antibodies can be obtained

- (a) Electron microscopy of negatively stained whole HtH, which has been purified by ultracentrifugation of cell-free haemolymph;
- (b) SDS polyacrylamide gel electrophoresis (7.5% polyacrylamide) of HtH1 compared with KLH (MW 370 kDa);
- (c) Native polyacrylamide gel electrophoresis (5% polyacrylamide) of the HtH subunit preparation, the anode being at the lower edge;
- (d) Crossed immunoelectrophoresis of the two HtH subunits using anti-HtH antibodies from the rabbit;
- (e) Electron microscopy of the remaining HtH1 didecamers (white arrows) after selective dissociation of HtH2 (black arrows);

- (f) Elution profile of the gel filtration chromatography (Biogel A15m) in the presence of ammonium molybdate/polyethylene glycol solution (pH 5.9) after selective dissociation of HtH2 into its subunit and subsequent concentration of HtH1 by ultracentrifugation;
- (g) Native polyacrylamide gel electrophoresis (6.5% polyacrylamide) of HtH1 and HtH2 subunits purified by gel chromatography compared with the starting material;
- (h,i) Crossed immunoelectrophoresis of chromatographically purified HtH subunits; and
- (j,m) Crossed immunoelectrophoresis of the purified HtH subunits using anti-KLH antibodies from the rabbit which are specific for KLH1 and KLH2.

Fig. 2 shows the analysis of the subunit organization of HtH1, anti-HtH1 antibodies from the rabbit having been used for the immunoelectrophoresis and the anode being on the left-hand side;

- (a) Crossed immunoelectrophoresis after limited proteolysis of HtH1 with the aid of elastase;
- (b) SDS polyacrylamide gel electrophoresis (7.5% polyacrylamide) of the elastase-cleaved HtH1 subunit;
- (c,d,g-j,l,n,p) Crossed immunoelectrophoresis of the elastase cleavage products of the HtH1 subunit;
- (e) Crossed immunoelectrophoresis after limited proteolysis of HtH1 with the aid of V8 protease;
- (f) SDS polyacrylamide gel electrophoresis (7.5% polyacrylamide) of the V8 protease-cleaved HtH1 subunit;
- (k,m,o) Crossed immunoelectrophoresis after limited proteolysis of HtH1 with the aid of the three stated proteases.

Fig. 3 shows the separation of proteolytic cleavage products of the subunit HtH1 with the aid of HPLC.

Fig. 4 shows the cDNA sequence of HtH1 in combination with the intron structure.

Fig. 5 shows the primary structure deduced for HtH1.

Fig. 6 shows the cDNA sequence of Hth2 in combination with the intron structure.

Fig. 7 shows the primary structure deduced for Hth2.

Fig. 8 shows the cDNA sequence of KLH1 in combination with the intron structure.

Fig. 9 shows the primary structure deduced for KLH1.

Fig. 10 shows the cDNA sequence of KLH2 in combination with the intron structure.

Fig. 11 shows the primary structure deduced for KLH2.

EXAMPLES

Material and methods

1. Preparation of the haemolymph and isolation of haemocyanin

Individuals of the European abalone *Haliotis tuberculata* from the French Atlantic coast region were provided by S.M.E.L (Blainville sur Mer, France) and Biosyn (Fellbach, Germany). The animals were kept in a 300 l sea-water aquarium at 17°C and fed with brown algae. For removal of the haemolymph, the abalones were placed on ice in a closed plastic bag. After one hour, large volumes of haemolymph had been secreted through their skin. It emerged that the haemocyanin obtained by this process is identical to the haemocyanin which could be collected by cutting a hollow in the foot of cooled-down sea snails using a scalpel blade. The blood cells were separated from the haemolymph by centrifugation at 800 g for 30 min at 4°C. The whole haemocyanin was then immediately sedimented by preparative ultracentrifugation at 30,000 g for 4 hours at 4°C. The supernatant was discarded and the blue haemocyanin pellet was suspended overnight in "stabilization buffer" (0.05 M Tris, 5 mM CaCl₂, 5 mM MgCl₂, 0.15 M NaCl, 1 mM PMSF, pH 7.4) and stored at 4°C.

Using the process described by Harris et al., 1995, supra, intact Hth1 was obtained from the whole Hth by selective dissociation of Hth2 in ammonium molybdate/polyethylene

glycol (1%/0.2%) solution, pH 5.9 and subsequent ultracentrifugation. The partly purified HtH1 pellet formed was dissolved and purified to homogeneity by gel filtration on a Biogel A15m device. The last step resulted in small amounts of purified HtH2. Native HtH1 and HtH2 was dissociated quantitatively into the subunits by dialysis against "dissociation buffer" (0.13 M glycine/NaOH, pH 9.6) at 4°C overnight; the presence of EDTA was not necessary. 1 mM PMSF was added at each stage of the purification to inhibit proteolysis.

2. Electron microscopy

Conventional "negative staining" was carried out by the individual drop method (Harris and Horne in Harris, J.R. (editors) *Electron microscopy in biology*, (1991), IRL Press Oxford, p. 203-228). Carbon carrier films were initially subjected to glow discharge for 20 seconds to render them hydrophilic and adsorptive for the protein. The protein samples are allowed to adsorb on to the carbon films for 60 seconds. The buffer salts are then removed by sequential washing with four successive 20 µl drops of water. Finally, the gratings are negatively stained with a 20 µl drop of 5% aqueous ammonium molybdate containing 1% trehalose (pH 7.0) and left to dry at room temperature. A Zeiss EM 900 transmission electron microscope is used for the electron microscopy analysis.

3. Polyacrylamide gel electrophoresis and immunoelectrophoresis

SDS polyacrylamide gel electrophoresis (SDS-PAGE) was carried out by the method of Laemmli (*Nature* 227 (1970), 670-685). An alkaline system according to Markl et al. (1979) *J. Comp. Physiol.* 133 B, 167-175 with a 0.33 M Tris/borate, pH 9.6 as the gel buffer and 0.065 M Tris/borate, pH 9.6 as the electrode buffer was used for the native PAGE. Crossed and "crossed-line" immunoelectrophoresis (IE) were carried out in accordance with Weeke (*Scand. J. Immunol.* 2 (1973), Suppl. 1, 47-56) or Kroll (*Scand. J. Immunol.* 2, Suppl. 1 (1973), 79-81). Rabbit antibodies against dissociated whole HtH and purified HtH1 were produced by Charles River Deutschland (Kisslegg, Germany). The immunization process was carried out in accordance with Markl and Winter (*J. Comp. Physiol.* 159B (1989), 139-151).

4. Limited proteolysis and isolation of the fragments

The limited proteolysis was carried out at 37°C in 0.13 M glycine/NaOH, pH 9.6 by addition of one of the following enzymes (Sigma, Deisenhofen, Germany), which were dissolved in 0.1 M NH_4HCO_3 , pH 8.0: *Staphylococcus aureus* V8 protease type XVII (8400), papain type II from papaya milk (P-3125), bovine pancreas elastase type IV (E-0258), chymotrypsin and trypsin. The haemocyanin concentration was between 1 and 10 mg/ml. The final concentration of the enzyme was 2% (weight/weight). The proteolysis was ended after 5 hours by freezing to -20°C. The HPLC process was carried out on a device from Applied Biosystems (BAI, Bensheim, Germany) equipped with a model 1000S Diode Array detector. The proteolytic fragments were introduced on to a small Mono-Q anion exchanger column (Pharmacia, Freiburg, Germany), which had been equilibrated with 0.02 M Tris/HCl, pH 8.0, and were eluted with a linear sodium chloride gradient (0.0 M – 0.5 M CaCl) in the same buffer at a flow rate of 1 ml/min. Alternatively, the proteolytic fragments were isolated by cutting out the bands from native PAGE gels (Markl et al., 1979) J. Comp. Physiol. **133** B, 167-175, after they had first been inversely stained with the Roti-White system (Roth, Karlsruhe, Germany) in accordance with Fernandez-Patron et al. (1995) Anal. Biochem. **224**, 203-211. For subsequent cleavage with a second enzyme, the fragments isolated were first dialysed overnight against 0.13 M glycine/NaOH, pH 9.6 to remove NaCl.

5. Amino acid sequence analysis

The proteins obtained by the HPLC process were denatured in SDS-containing sample buffer and separated by SDS-PAGE (Laemmli, 1970, supra; 7.5 % polyacrylamide). To prevent blocking of the NH_2 terminus, 0.6% (weight/weight) thioglycolic acid was added to the cathode buffer (Walsh et al., Biochemistry **27** (1988), 6867-6876). The protein bands were transferred by electro-transfer to ProBlot membranes (Applied Biosystems, Germany) in a vertical blotting chamber (25 mM borate buffer, pH 8.8, containing 2 mM EDTA; 10 min/100 mA, 15 min/200 mA, 12 h/300 mA). Detection of the individual polypeptides on the membranes was carried out with Ponceau S stain. The polypeptide bands of interest were cut out and sequenced in a 477A protein sequencing device from Applied Biosystems. The amounts of polypeptides applied to the sequencing device were in the lower pmol range.

6. cDNA cloning and sequence analysis

A lambda-cDNA expression library was established from poly(A⁺)-RNA from *Haliotis* mantle tissue using the vector Lambda ZAP Express[®] in accordance with the manufacturer's instructions (Stratagene, Heidelberg, Germany). The clones were isolated using HtH-specific rabbit antibodies. The nucleotide sequencing was carried out on both strands using the Taq Dye deoxy Terminator[®] system. The sequences were arranged with the software CLUSTAL W (1.7)[®] and TREEVIEW[®] (Thompson et al., Nucl. Acids Res. 22 (1994), 4673-4680).

Example 1:

Isolation of HtH and separation of two different types (HtH1 and HtH2)

The haemolymph was obtained from adult abalones. The blood cells were removed by centrifugation and the haemocyanin was then sedimented by ultracentrifugation. The blue haemocyanin pellet was dissolved again in "stabilization buffer" (pH 7.4) and examined by electron microscopy (figure 1a). It comprised mainly typical di-decamers, accompanied by a small content of decamers and tridecamers. Denaturing in 2% SDS in the presence of reducing substances and subsequent SDS-PAGE separation resulted in a single band, which corresponded to the polypeptide with an apparent molecular weight of 370 kDa, which is only slightly below the apparent subunit weight of KLH (figure 1b). Complete dissociation of the oligomers and of the di-decamers into the native polypeptides (subunits) was achieved by overnight dialysis of HtH against "dissociation buffer" (pH 9.6). The native PAGE method, which was used on these samples, showed a main and a secondary component (figure 1c). Crossed immunoelectrophoresis (crossed IE) using polyclonal rabbit antibodies generated against purified whole HtH showed two components which are immunologically different but show the classical reaction of being partly immunologically identical (figure 1d). Their preparative isolation (figure 1e-i) showed that they are subunits of two different HtH types, called HtH1 and HtH2, and the patterns of the native PAGE and crossed IE methods could be assigned to each individually (figure 1c, d).

The separation of HtH1 and HtH2 was carried out by the method of selective dissociation according to Harris et al., 1995, *supra*. In ammonium molybdate/polyethylene glycol, HtH1 in the oligomer state (di-decamer) was completely stable, while HtH2 dissociated completely into the subunits (figure 1e). This allowed quantitative sedimentation of HtH1 in an ultracentrifuge, while the majority of the HtH2 remained in the supernatant. Large amounts of HtH1 were purified to homogeneity from the redissolved pellet by gel filtration chromatography, which also resulted in small amounts of pure HtH2 (figure 1f). The fractions were investigated by native PAGE (figure 1g) and crossed IE (figure 1h, i). The process of selective dissociation of HtH2 removed all the tri-decamer from the samples, which suggests that the latter are built up from HtH2, but not from HtH1 (figure 1e). The selective dissociation behaviour of HtH2 and also the ability to form aggregates which are larger than *in vivo* di-decamers correspond to the properties of KLH2. Conversely, the stability of HtH1 under these conditions and its inability to assemble into aggregates larger than di-decamers resemble the behaviour of KLH1. This feature of being related is demonstrated further by the reaction of anti-KLH1 and anti-KLH2 antibodies against the two HtH types (figure 1j-m).

Example 2:

Analysis of the organization of the HtH1 subunit

The eight functional units (FUs, often called "functional domains") which form a mollusc haemocyanin subunit differ in primary structure and show no immunological cross-reactivity, as emerged from crossed IE. In the case of the purified HtH1 subunit (Figure 1g, h), small concentrations of five different proteases (elastase, V8 protease, papain, trypsin and chymotrypsin) which had cleaved the peptide bonds between adjacent FUs of KLH1 and KLH2 were used (Gebauer et al., 1994, *supra*, Söhnngen et al., 1997, *supra*). The cleavage products were investigated by crossed IE and SDS-PAGE (Fig. 2). Elastase treatment produces eight individual FUs, deduced from the number of different immunoprecipitation peaks in the crossed IE (Fig. 2a) and with the apparent molecular weight of approx. 50 kDa of the main portion of the cleavage products in SDS-PAGE (Fig. 2b). A further precipitation peak was recognized as FU dimer, which was formed by incomplete cleavage of the segment ab (Fig. 2a). By an HPLC process with a Mono-Q column (Fig. 3a), two of the elastase cleavage products

were obtained in a sufficient purity to allow their clear assignment to two of the eight precipitation peaks (Fig. 2c, d) by "crossed-line IE". The other four proteases had different cleavage patterns, which comprised mixtures of individual FUs and larger fragments containing two, three or more FUs (e.g. Fig. 2e, f). Many of them were concentrated to a sufficient amount by the HPLC process (Fig. 3b-e) to allow their identification in their corresponding SDS-PAGE and crossed IE patterns. A number of these components were sequenced N-terminally by blot transfer of SDS gels on ProBlot® membranes (Table 1). The results were compared with the N-terminal sequences which had been obtained from the apparently orthologous protein in *Megathura crenulata*, KLH1 (Table I), the complete FU arrangement of which is available (Söhngen et al., 1997, supra; cf. Fig. 5b). The result of the entire batch led to the determination of the complete FU arrangement within the HtH1 subunit (Fig. 2a).

In particular, cleavage of the HtH1 subunit (1-abcdefgh) with V8 protease resulted in four precipitation peaks in the crossed IE (Fig. 2e). The SDS-PAGE showed five different fragments (Fig. 2f): 220 kDa (5 FUs), 185 kDa (4 FUs), 100 kDa (2 FUs), 55 kDa (1 FU) and 46 kDa (1 FU). The 100 kDa fragment was isolated by the HPLC method (Fig. 3b) and identified by N-terminal sequencing as 1-ab, since the sequence was identical to that of the intact subunit (Table I). In the "crossed-line" IE process, 1-ab fused with three precipitation peaks of the elastase cleavage pattern. On the basis of the evaluation, they represent fragments 1-ab, 1-a and 1-b (Fig. 2g). However, it remained unclear which peak represents 1-a and which 1-b. In a second step, the 1-ab purified by HPLC was cleaved by elastase into its component FUs, from which one could be eluted by the native PAGE gel strip method and was assigned to the elastase pattern by the "crossed-line" IE method (Fig. 2h) and sequenced N-terminally. This component had the same N-terminal sequence as the whole subunit and was therefore identical to 1-a. The second FU of the 100 kDa fragment is thus 1-b (Fig. 2a; Table I). HPLC-purified 1-c and 1-h were also obtained (Fig. 3b), identified by N-terminal sequence similarities with the corresponding FUs in KLH1 (Table I) and assigned by the "crossed-line" IE method to their corresponding precipitation peaks in the elastase pattern (Fig. 2i, j). 1-a, 1-b, 1-c and 1-h were furthermore identified (Fig. 2a). Using papain for subunit cleavage, five different peaks were obtained in the crossed IE method (Fig. 2k). A 100 kDa fragment (2 FUs) was purified from such a sample by the HPLC method (Fig. 3c), and, according to the "crossed-line" IE method, contained the FU 1-h already identified and one of the four

FUs still not identified and therefore must be 1-gh (Fig. 2k, 3c). In fact, this fragment had an N-terminal sequence which showed similarities with KLH1-g (Table I). For further confirmation, the HPLC-purified fragment 1-gh was cleaved into its constituent FUs with elastase, from which 1-g was purified and identified by N-terminal sequencing. It was assigned to its peak in the elastase cleavage pattern by the "crossed-line" IE method (Fig. 2l).

The 220 kDa fragment from the V8 protease cleavage (Fig. 2e, f) was purified by HPLC (Fig. 3b) and in the "crossed-line" IE method fused with 1-h, 1-g and three peaks of the elastase cleavage pattern which have not yet been identified. The 185 kDa fragment was furthermore obtained in a sufficient purity (Fig. 2e, f; 3b), and it was shown that it comprised the same components with the exception of 1-h. This suggested that the 22 kDa and the 185 kDa fragment are 1-defgh and 1-defg respectively. In fact, the N-terminal sequence was practically identical and furthermore showed similarity with KLH1-d (Table I). Cleavage of the HtH1 subunit with trypsin resulted in a large number of components in the molecular weight range of one or two FUs (Fig. 2m). Several of the components were concentrated in HPLC fractions (Fig. 3d). A 100 kDa fragment proved to be particularly useful since it had the same N-terminal sequence as the fragment 1-defg from the v8 protease cleavage (Table I); the 100 kDa fragment should therefore be 1-de. In the "crossed-line" IE method, this component fused with two of the three FU peaks of the elastase cleavage pattern not yet identified (Fig. 2n), which should therefore be 1-d and 1-e, and thus left a single possibility for 1-f. The "crossed-line" IE method also showed that FU 1-f was furthermore present in the 1-de fraction (Fig. 2n). The identification of 1-f was confirmed by cleavage of the subunit with chymotrypsin (Fig. 2o) and a subsequent HPLC process (Fig. 3e). This cleavage gave, inter alia, a 95 kDa fragment (2 FUs) which fused with 1-g and a second peak (Fig. 2p) in the "crossed-line" IE method and could therefore be either 1-gh (which could be ruled out since 1-h had already been identified) or 1-fg (which seems appropriate on the basis of the further peak in question, which was identical to the remaining candidate). In fact, this fragment showed a new N-terminal sequence which is similar to KLH1-f in a certain manner. The last problem was now to assign the two remaining FU peaks to 1-d and 1-e. This was achieved using HPLC-isolated FUs from samples in which the subunit had been cleaved with elastase. (Fig. 2c, d; 3a). The more acidic component in the crossed IE method was deduced as 1-d from its N-terminal sequence, which is identical to that of 1-defgh (Fig.

2c, Table I), while the more basic component of the 1-d/1-g pair had a new N-terminal sequence (Table I) and therefore had to be 1-e (Fig. 2a). The structure of the functional units of subunit HtH1 was thus clarified.

Example 3:

Comparison of the molecular weights and N-terminal sequences of the biochemically isolated functional units (FUs) from HtH1 and KLH1. The various FUs, each with an intact binuclear copper-binding site, were liberated from their larger unit as globular segments by limited proteolysis; cf. the section "Isolation and analysis of the units from HtH1". The KLH1 data were obtained from Söhnngen et al., *supra*. The assignment as an actual unit was done on the basis of the molecular weight and the immunological properties (cf. Fig. 2). The unusually low molecular weight of isolated HtH1-d could mean that a large peptide was split off C-terminally.

TABLE 1

Functional unit	Weight (kDa)	N-terminal sequence
HtH1-a	53	DNV VR KDVSHLTDDEVQ
KLH1-a	50	ENL VR KDVERL
HtH1-b	48	?
KLH1-b	45	?
HtH1-c	46	FEDEKHSLR IR KNVDSLTPPEENTNERLR
KLH1-c	45	KVPRSRL IR KNVDRLTPSE
HtH1-d	40	VEEVTGASH IR KNLNDLNTGEM
KLH1-d	50	EVTSANR IR KNIENLS
HtH1-e	49	ILDHDHEEEIL VR KNIIDLSP
KLH1-e	50	?
HtH1-f	50	KLNSRKHTPNR VR HELSSLSSRDIASLKA
KLH1-f	45	HHLSXNK VR HDLSTL
HtH1-g	45	DHQSGSIAGSG VR KDVNTLTKAETDNLRE
KLH1-g	45	SSMAGHF VR KDINTLTP
HtH1-h	55	DEHHDDRDLADVLR IR KEVDFLSLQEANAIDK
KLH1-h	60	HEDHHEDIL VR KNIHSL

Example 4:**Cloning of haemocyanin cDNA**

1. For cloning the cDNA of haemocyanin, mRNA was isolated from the mantle tissue of the particular mollusc. The first cDNA strand was obtained by reverse transcription with Oligo(dT) as a primer. The second strand was obtained conventional synthesis with random primers. The cDNA obtained in this way was cloned in a lambda expression vector to form a cDNA expression library. Using an anti-haemocyanin antibody, the library was searched under suitable conditions, positive clones being obtained. These positive clones were isolated, sequenced and characterized.

2. A cDNA probe was prepared from the N-terminal region of a positive clone obtained, and the cDNA library was searched with this. The positive clones obtained were in turn isolated, sequenced and characterized.
3. To obtain sequences arranged still further to 5', another expression library was established from cDNA, this being obtained with the aid of a combination of haemocyanin-specific and "random" primers. This cDNA library was searched with cDNA probes which correspond to the "N-terminal" regions of the positive clones obtained under (2.). The positive clones obtained were isolated, sequenced and characterized.

Example 5:

Cloning of haemocyanin genes

Genomic DNA was isolated by standard methods. The PCR reaction was carried out with the aid of haemocyanin-specific primers in order to amplify the gene sections of the haemocyanins of interest. The amplification products obtained were cloned in a suitable vector (for example pGem T or pGem T easy (Promega, Mannheim) sequenced and characterized.

Example 6:

Recombinant expression of haemocyanin

A PCR reaction was carried out with a cDNA clone which contains the coding sequence for HtH-1d in order to amplify specifically the coding sequence of the domain 1d.

Synthetically prepared oligonucleotides were used as primers.

Primer 1 (upstream) comprises six nucleotides of the end of the domain HtH-1c, an *SacI* cleavage site and 12 nucleotides of the end of the domain HtH-1d.

Primer 2 (downstream) comprises six nucleotides of the start of the domain HtH-1e, an *SalI* cleavage site and an HtH1-d-specific sequence.

PCR conditions:

2	min	95°C
30	sec	95°C
30	sec	55°C
1	min	72°C
35	cycles	
10	min	72°C

The amplification product was cloned in the pGEM T easy PCR cloning vector (Promega) in XL-1 Blue (Stratagene). After isolation of the recombinant plasmid and restriction with *SacI* and *SalI*, the cDNA of domain 1d could be isolated. The expression vector pQE30 (Qiagen) was also restricted with the corresponding enzymes.

The ligation was then carried out between the Hth-1d-cDNA (restricted with *SacI* and *SalI*) and pQE (restricted with *SacI* and *SalI*). Directed cloning of the cDNA which codes for Hth-1d in an expression vector is thus possible. The expression of Hth1-d in pQE in XL-1 Blue is carried out in accordance with the manufacturer's instructions. The expression of further Hth1, Hth2 or KLH1 or KLH2 domains can be carried out analogously.

Preliminary Amendment -1-

Clean Copy of Amendments

Markl, et al.

§ 371 Patent Application of PCT/EP00/02410
filed September 17, 2001

WHAT IS CLAIMED IS:

1. Nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),

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SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),

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SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerate to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

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- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).

2. Nucleic acid molecule according to claim 1, **characterized in that** the hybridization described under (b) or (d) is carried out under stringent conditions.

3. Nucleic acid molecule according to claim 1,
characterized in that the nucleic acid molecule
described under (e) is at least 80% homologous to one
of the nucleic acid sequences described under (a).

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4. Nucleic acid molecule according to claim 1, **characterized in that** the nucleic acid molecule described under (e) is at least 90 % homologous to one of the nucleic acid sequences described under (a).

5. Nucleic acid molecule according to claim 1, **characterized in that** the nucleic acid molecule described under (e) is at least 95 % homologous to one of the nucleic acid sequences described under (a).

6. Nucleic acid molecule according to claim 1,
characterized in that it is a deoxyribonucleic acid
molecule.

7. Construct comprising a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),

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SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),

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SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin;

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and

(g) combinations of several of the DNA sequences described under (a) to (f)

8. Construct according to claim 7, further comprising a promoter which is suitable for expression control, the nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof being under the control of the promoter.

9. Construct according to claim 7, further comprising a nucleic acid sequence which codes for an antigen and is coupled directly to the nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof.

10. Construct according to claim 9, wherein the antigen is selected from: tumour antigens, virus antigens and antigens of bacterial or parasitic pathogens.

11. Construct according to claim 7, wherein the construct comprises at least a part of a vector, the vector being selected from: bacteriophages, adenoviruses, vaccinia viruses, baculoviruses, SV40 virus and retroviruses.

12. Construct according to claim 7, wherein the

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SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

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- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).

14. Host cell according to claim 13, **characterized in that** the prokaryotic host cell is selected from E. coli and Bacillus subtilis.

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15. Host cell according to claim 13, **characterized in that** the eukaryotic host cell is selected from yeast cells, plant cells, insect cells and mammalian cells, preferably from CHO cells, COS cells and HeLa cells.

16. Process for the preparation of a haemocyanin polypeptide, wherein a nucleic acid molecule and/or a construct comprising said nucleic acid molecule is expressed in a suitable host cell and the protein is isolated, if appropriate, wherein said nucleic acid molecule comprising a nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),

SEO ID NO:2 (HtH1 domain b),

SEQ ID NO:3 (HtH1 domain c),

SEQ ID NO:4 (HtH1 domain d),

SEQ ID NO:5 (HtH1 domain e),

SEQ ID NO:6 (HtH1 domain f),

SEQ ID NO:7 (HtH1 domain g),

SEQ ID NO: 8 (HtH1 domain h),

SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),

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SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

(b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence

according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin;
and
- (g) combinations of several of the DNA sequences described under (a) to (f).

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that the haemocyanin polypeptide prepared is modified naturally or chemically.

18. Process according to claim 17, **characterized in that** the modification is a crosslinking or a covalent bonding to an antigen.

19. Process according to claim 16, **characterized in that** the expression is carried out in a host cell.

20. Haemocyanin polypeptide, comprising an amino acid sequence which is coded by one or more of a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),

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counter-strand of a nucleic acid sequence
according to (a) and code for a polypeptide which
has the immunological properties of at least one
domain of a haemocyanin;

(c) nucleic acid sequences which on the basis of the
genetic code are degenerated to the DNA sequences
defined under (a) and (b) and code for a
polypeptide which has the immunological properties
of at least one domain of a haemocyanin;

(d) nucleic acid sequences which hybridize with one
of the nucleic acid sequences described under (a)
to (c) and the counter-strand of which codes for a
polypeptide which has the immunological properties
of at least one domain of a haemocyanin;

(e) nucleic acid sequences which are at least 60%
homologous to one of the nucleic acid sequences
described under (a);

(f) variants of the sequences described under (a) to
(d), the variants containing additions, deletions,
insertions or inversions with respect to the
sequences described under (a) to (d) and coding
for a polypeptide which has the immunological
properties of at least one domain of haemocyanin;
and

(g) combinations of several of the DNA sequences
described under (a) to (f).

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21. Haemocyanin polypeptide according to claim 20, comprising at least one amino acid sequence selected from the following group:

SEQ ID NO:25 (HtH1 domain a + signal peptide),
SEQ ID NO:26 (HtH1 domain b),
SEQ ID NO:27 (HtH1 domain c),
SEQ ID NO:28 (HtH1 domain d),
SEQ ID NO:29 (HtH1 domain e),
SEQ ID NO:30 (HtH1 domain f),
SEQ ID NO:31 (HtH1 domain g),
SEQ ID NO:32 (HtH1 domain h),
SEQ ID NO:33 (partial HtH2 domain b),
SEQ ID NO:34 (HtH2 domain c),
SEQ ID NO:35 (HtH2 domain d),
SEQ ID NO:36 (HtH2 domain e),
SEQ ID NO:37 (HtH2 domain f),
SEQ ID NO:38 (HtH2 domain g),
SEQ ID NO:39 (HtH2 domain h),
SEQ ID NO:40 (partial KLH1 domain b),
SEQ ID NO:41 (KLH1 domain c),
SEQ ID NO:42 (partial KLH1 domain d),
SEQ ID NO:43 (partial KLH1 domain e),
SEQ ID NO:44 (KLH2 domain b),
SEQ ID NO:45 (KLH2 domain c),
SEQ ID NO:46 (partial KLH2 domain d),
SEQ ID NO:47 (KLH2 domain g),
SEQ ID NO:48 (partial KLH2 domain h),
SEQ ID NO:63 (HtH1 domain a' + signal peptide),
SEQ ID NO:64 (HtH1 domain h'),
SEQ ID NO:65 (partial HtH2 domain a),

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SEQ ID NO:66 (HtH2 domain b'),
SEQ ID NO:67 (HtH2 domain d'),
SEQ ID NO:68 (HtH2 domain e'),
SEQ ID NO:69 (partial KLH1 domain b'),
SEQ ID NO:70 (KLH1 domain e'),
SEQ ID NO:71 (KLH1 domain f),
SEQ ID NO:72 (KLH1 domain g),
SEQ ID NO:73 (KLH1 domain h),
SEQ ID NO:74 (KLH2 domain b'),
SEQ ID NO:75 (KLH2 domain c'),
SEQ ID NO:76 (KLH2 domain d'),
SEQ ID NO:77 (KLH2 domain e),
SEQ ID NO:78 (KLH2 domain f),
SEQ ID NO:79 (KLH2 domain g'),

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or a fragment of one of these sequences which has the immunological properties of at least one domain of a haemocyanin.

22. Recombinant haemocyanin polypeptide, obtainable by a process for the preparation of a haemocyanin polypeptide, wherein a nucleic acid molecule and/or a construct comprising said nucleic acid molecule is expressed in a suitable host cell and the protein is isolated, if appropriate, wherein said nucleic acid molecule comprising a nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

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(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),

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SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),

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SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences

(f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and

23. Recombinant haemocyanin polypeptide according to claim 22, **characterized in that** it comprises the sequences SEQ ID NO: 25 to 32 and is haemocyanin 1 from *Haliotis tuberculata*, it being possible for the sequence with SEQ ID NO:25 to be replaced by SEQ ID NO:63 and/or SEQ ID NO:32 to be replaced by SEQ ID NO:64.

25. Recombinant haemocyanin polypeptide according to claim 23, **characterized in that** it has an apparent

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molecular weight of 370 kDa in SDS-PAGE under
reducing conditions.

26. Recombinant haemocyanin polypeptide according to
claim 24, **characterized in that** it has an apparent
molecular weight of 370 kDa in SDS-PAGE under
reducing conditions.

27. Recombinant haemocyanin polypeptide according to
claim 21, **characterized in that** the haemocyanin
polypeptide comprises either the sequences SEQ ID NO:
40 to 43 or the sequences SEQ ID NO:40 to 43 and SEQ
ID NO:71 to 73 and is KLH1 from *Megathura crenulata*,
it being possible in each case the for sequence with
SEQ ID NO:40 to be replaced by SEQ ID NO:66 and/or
SEQ ID NO:43 to be replaced by SEQ ID NO:70.

28. Recombinant haemocyanin polypeptide according to
claim 21, **characterized in that** the haemocyanin
polypeptide comprises either the sequences SEQ ID NO:
44 to 48 or the sequences SEQ ID NO:44 to 46, 77, 78,
47, 48 and is KLH2 from *Megathura crenulata*, in being
possible in each case for the sequence with SEQ ID
NO:44 to be replaced by SEQ ID NO:74, SEQ ID NO:45 to
be replaced by SEQ ID NO:75, SEQ ID NO:46 to be
replaced by SEQ ID NO:76 and/or SEQ ID NO:47 to be
replaced by SEQ ID NO:79.

29. Recombinant haemocyanin polypeptide according to
claim 20, **characterized in that** it is bonded
covalently to viruses, virus constituents, bacteria,

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bacteria constituents, DNA, DNA constituents,
inorganic or organic molecules, such as e.g.
carbohydrates, peptides and/or glycoproteins.

30. Recombinant haemocyanin polypeptide according to
claim 20, **characterized in that** the haemocyanin
polypeptide is non-glycosylated.

31. Recombinant haemocyanin polypeptide according to
claim 20, **characterized in that** the haemocyanin
polypeptide is glycosylated.

32. Pharmaceutical composition, comprising a nucleic
acid molecule and/or a construct comprising said
nucleic acid molecule and physiologically tolerated
additives, wherein said nucleic acid molecule
comprises a nucleic acid sequence which codes for a
haemocyanin, a haemocyanin domain or a functional
fragment thereof with the immunological properties of
at least one domain of a haemocyanin, the nucleic
acid sequence being selected from:

(a) nucleic acid sequences which are selected from
the group consisting of the DNA sequences shown
below or the corresponding RNA sequences or which
contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),

SEQ ID NO:2 (HtH1 domain b),

SEQ ID NO:3 (HtH1 domain c),

SEQ ID NO:4 (HtH1 domain d),

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SEQ ID NO:5 (HtH1 domain e),
 SEQ ID NO:6 (HtH1 domain f),
 SEQ ID NO:7 (HtH1 domain g),
 SEQ ID NO: 8 (HtH1 domain h),
 SEQ ID NO:9 (partial HtH2 domain b),
 SEQ ID NO:10 (HtH2 domain c),
 SEQ ID NO:11 (HtH2 domain d),
 SEQ ID NO:12 (HtH2 domain e),
 SEQ ID NO:13 (HtH2 domain f),
 SEQ ID NO:14 (HtH2 domain g),
 SEQ ID NO:15 (HtH2 domain h),
 SEQ ID NO:16 (partial KLH1 domain b),
 SEQ ID NO:17 (KLH1 domain c),
 SEQ ID NO:18 (KLH1 domain d),
 SEQ ID NO:19 (partial KLH1 domain e),
 SEQ ID NO:20 (KLH2 domain b),
 SEQ ID NO:21 (KLH2 domain c),
 SEQ ID NO:22 (partial KLH2 domain d),
 SEQ ID NO:23 (KLH2 domain g),
 SEQ ID NO:24 (partial KLH2 domain h),
 SEQ ID NO:49 (HtH1 domain a' + signal peptide),
 SEQ ID NO:50 (partial HtH2 domain a),
 SEQ ID NO:51 (HtH2 domain b'),
 SEQ ID NO:52 (HtH2 domain d'),
 SEQ ID NO:53 (HtH2 domain e'),
 SEQ ID NO:54 (KLH1 domain e'),
 SEQ ID NO:55 (KLH1 domain f),
 SEQ ID NO:56 (KLH1 domain g),
 SEQ ID NO:57 (KLH2 domain b'),
 SEQ ID NO:58 (KLH2 domain c'),
 SEQ ID NO:59 (KLH2 domain d'),

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SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),

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(g) combinations of several of the DNA sequences described under (a) to (f).

33. Pharmaceutical composition according to claim 32, **characterized in that** it is used for gene therapy treatment of tumours.

34. Pharmaceutical composition, comprising a haemocyanin polypeptide according to claim 20 and physiologically tolerated additives, wherein said haemocyanin polypeptide comprises an amino acid sequence which is coded by one or more of the nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),

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SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),

(b) nucleic acid sequences which hybridize with the

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counter-strand of a nucleic acid sequence
according to (a) and code for a polypeptide which
has the immunological properties of at least one
domain of a haemocyanin;

(c) nucleic acid sequences which on the basis of the
genetic code are degenerated to the DNA sequences
defined under (a) and (b) and code for a
polypeptide which has the immunological properties
of at least one domain of a haemocyanin;

(d) nucleic acid sequences which hybridize with one
of the nucleic acid sequences described under (a)
to (c) and the counter-strand of which codes for a
polypeptide which has the immunological properties
of at least one domain of a haemocyanin;

(e) nucleic acid sequences which are at least 60%
homologous to one of the nucleic acid sequences
described under (a);

(f) variants of the sequences described under (a) to
(d), the variants containing additions, deletions,
insertions or inversions with respect to the
sequences described under (a) to (d) and coding
for a polypeptide which has the immunological
properties of at least one domain of haemocyanin;
and

(g) combinations of several of the DNA sequences
described under (a) to (f).

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35. Pharmaceutical composition according to claim 34, **characterized in that** it is used as an antiparasitic composition, antiviral composition or as an antitumour composition.

36. Pharmaceutical composition according to claim 34, **characterized in that** it is used for treatment of one of the following diseases: schistosomiasis, high blood pressure, surface bladder carcinomas, epithelial carcinomas, ovarian carcinoma, mammary carcinoma, bronchial carcinoma and colorectal carcinoma.

37. Pharmaceutical composition according to claim 34, **characterized in that** it is used as a vaccine.

38. Pharmaceutical composition according to claim 34, **characterized in that** it is used for prevention of cocaine abuse.

39. Use of a haemocyanin polypeptide as a carrier substance for medicaments, wherein said haemocyanin polypeptide comprises an amino acid sequence which is coded by one or more of the nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from

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the group consisting of the DNA sequences shown
below or the corresponding RNA sequences or which
contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),

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SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),

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(f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and

(g) combinations of several of the DNA sequences described under (a) to (f).

40. Liposome, comprising a nucleic acid molecule , a construct comprising said nucleic acid molecule and/or a haemocyanin polypeptide encoded by said nucleic acid molecule, wherein said nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),

SEQ ID NO:2 (HtH1 domain b),

SEQ ID NO:3 (HtH1 domain c),

SEQ ID NO:4 (HtH1 domain d),

SEQ ID NO:5 (HtH1 domain e),

SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerate to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences

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described under (a) to (f).

41. Liposome according to claim 40, **characterized in that** the liposome furthermore comprises cell recognition molecules.

42. Antibodies, obtainable by immunization of a test animal with a recombinant haemocyanin polypeptide comprising an amino acid sequence which is coded by one or more of the nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),

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SEQ ID NO:11 (HtH2 domain d),
 SEQ ID NO:12 (HtH2 domain e),
 SEQ ID NO:13 (HtH2 domain f),
 SEQ ID NO:14 (HtH2 domain g),
 SEQ ID NO:15 (HtH2 domain h),
 SEQ ID NO:16 (partial KLH1 domain b),
 SEQ ID NO:17 (KLH1 domain c),
 SEQ ID NO:18 (KLH1 domain d),
 SEQ ID NO:19 (partial KLH1 domain e),
 SEQ ID NO:20 (KLH2 domain b),
 SEQ ID NO:21 (KLH2 domain c),
 SEQ ID NO:22 (partial KLH2 domain d),
 SEQ ID NO:23 (KLH2 domain g),
 SEQ ID NO:24 (partial KLH2 domain h),
 SEQ ID NO:49 (HtH1 domain a' + signal peptide),
 SEQ ID NO:50 (partial HtH2 domain a),
 SEQ ID NO:51 (HtH2 domain b'),
 SEQ ID NO:52 (HtH2 domain d'),
 SEQ ID NO:53 (HtH2 domain e'),
 SEQ ID NO:54 (KLH1 domain e'),
 SEQ ID NO:55 (KLH1 domain f),
 SEQ ID NO:56 (KLH1 domain g),
 SEQ ID NO:57 (KLH2 domain b'),
 SEQ ID NO:58 (KLH2 domain c'),
 SEQ ID NO:59 (KLH2 domain d'),
 SEQ ID NO:60 (KLH2 domain e),
 SEQ ID NO:61 (KLH2 domain f),
 SEQ ID NO:62 (KLH2 domain g'),
 SEQ ID NO:80 (HtH1 domain a" + signal peptide),
 SEQ ID NO:81 (HtH1 domain b"),
 SEQ ID NO:82 (HtH1 domain c"),

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SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one

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domain of a haemocyanin;

- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).

43. Screening method for identification of tumour-specific DNA in a cell, comprising:

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A. bringing cell DNA and/or cell protein into contact with a probe comprising a nucleic acid molecule and/or the antibody obtainable by immunization of a test animal with a recombinant haemocyanin polypeptide comprising an amino acid sequence which is coded by one or more of said nucleic acid molecules, wherein said nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),

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SEQ ID NO:14 (HtH2 domain g),
 SEQ ID NO:15 (HtH2 domain h),
 SEQ ID NO:16 (partial KLH1 domain b),
 SEQ ID NO:17 (KLH1 domain c),
 SEQ ID NO:18 (KLH1 domain d),
 SEQ ID NO:19 (partial KLH1 domain e),
 SEQ ID NO:20 (KLH2 domain b),
 SEQ ID NO:21 (KLH2 domain c),
 SEQ ID NO:22 (partial KLH2 domain d),
 SEQ ID NO:23 (KLH2 domain g),
 SEQ ID NO:24 (partial KLH2 domain h),
 SEQ ID NO:49 (HtH1 domain a' + signal peptide),
 SEQ ID NO:50 (partial HtH2 domain a),
 SEQ ID NO:51 (HtH2 domain b'),
 SEQ ID NO:52 (HtH2 domain d'),
 SEQ ID NO:53 (HtH2 domain e'),
 SEQ ID NO:54 (KLH1 domain e'),
 SEQ ID NO:55 (KLH1 domain f),
 SEQ ID NO:56 (KLH1 domain g),
 SEQ ID NO:57 (KLH2 domain b'),
 SEQ ID NO:58 (KLH2 domain c'),
 SEQ ID NO:59 (KLH2 domain d'),
 SEQ ID NO:60 (KLH2 domain e),
 SEQ ID NO:61 (KLH2 domain f),
 SEQ ID NO:62 (KLH2 domain g'),
 SEQ ID NO:80 (HtH1 domain a" + signal peptide),
 SEQ ID NO:81 (HtH1 domain b"),
 SEQ ID NO:82 (HtH1 domain c"),
 SEQ ID NO:83 (HtH1 domain d"),
 SEQ ID NO:84 (HtH1 domain e"),
 SEQ ID NO:85 (HtH1 domain f"),

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colorectal carcinoma.

[illegible]

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Fig. 1a-f

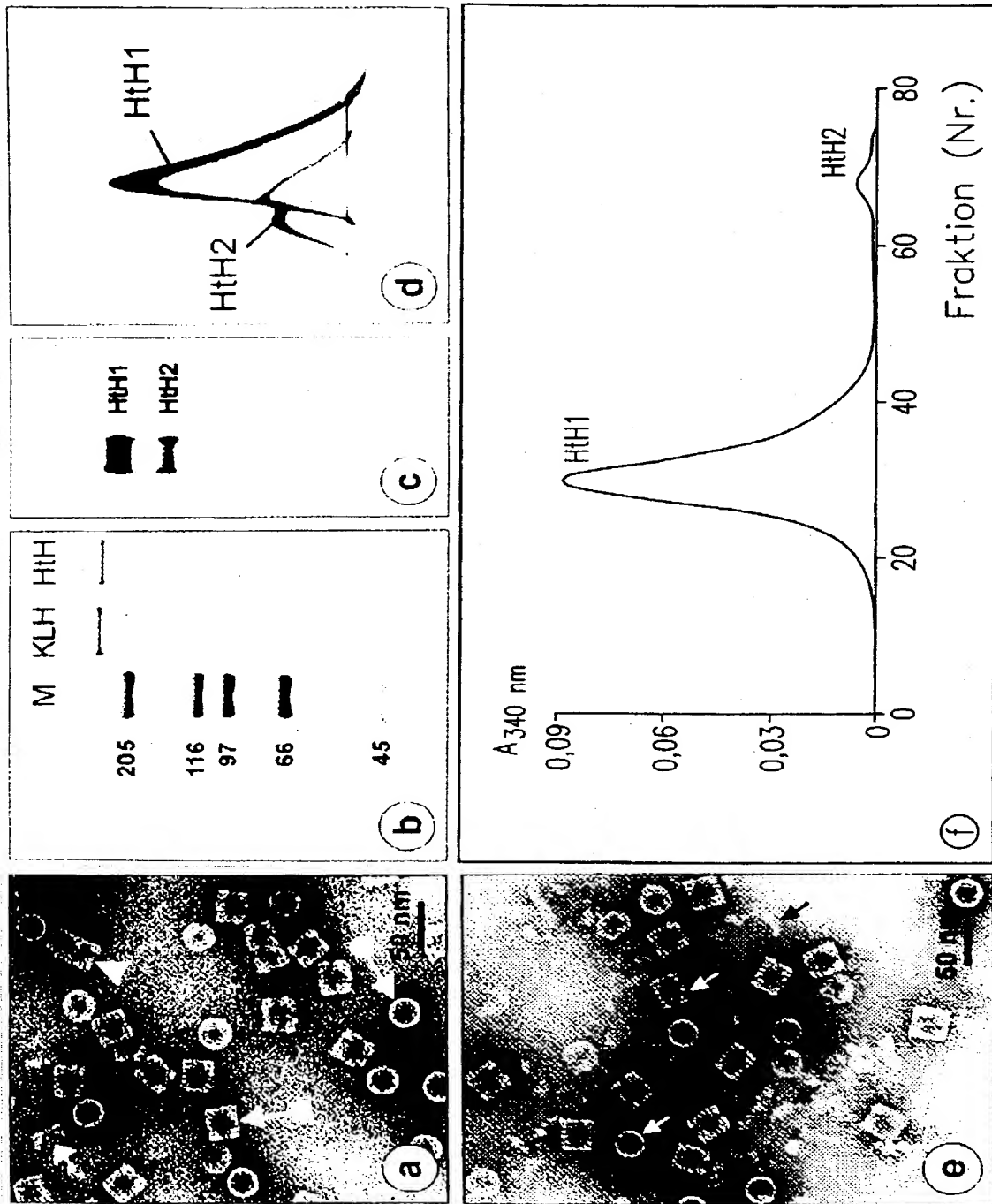


Fig. 1g-m

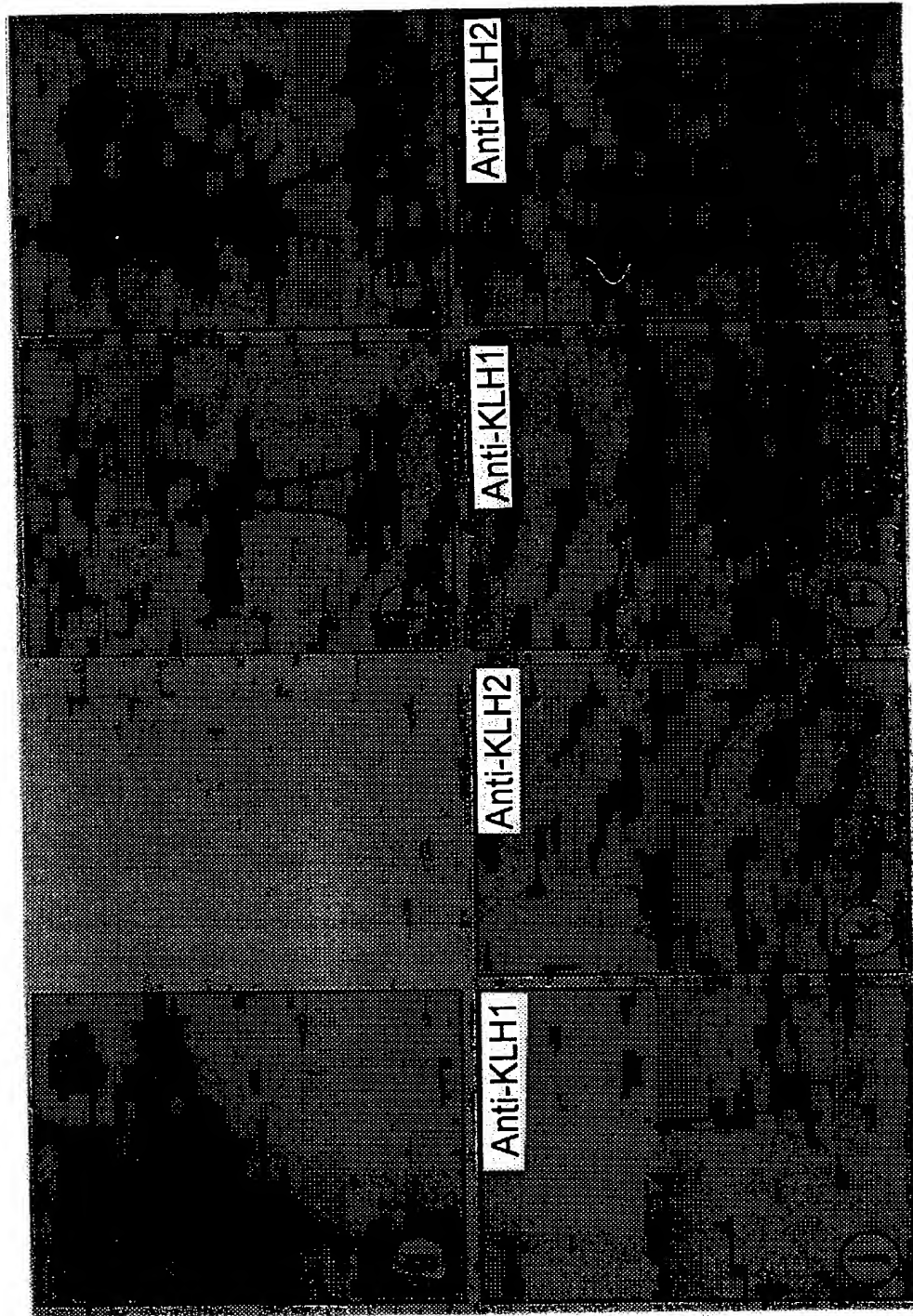


Fig. 2a-h

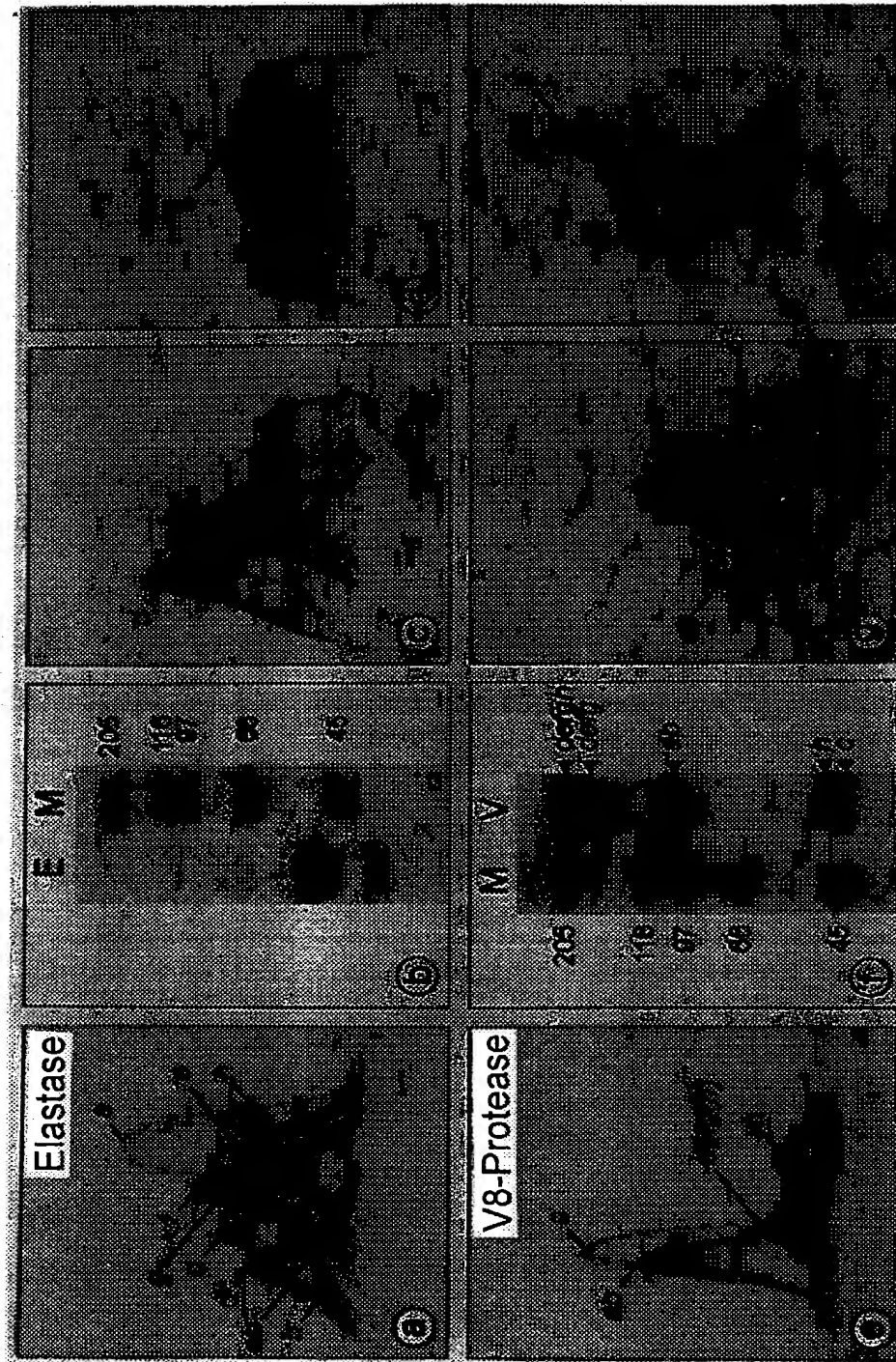
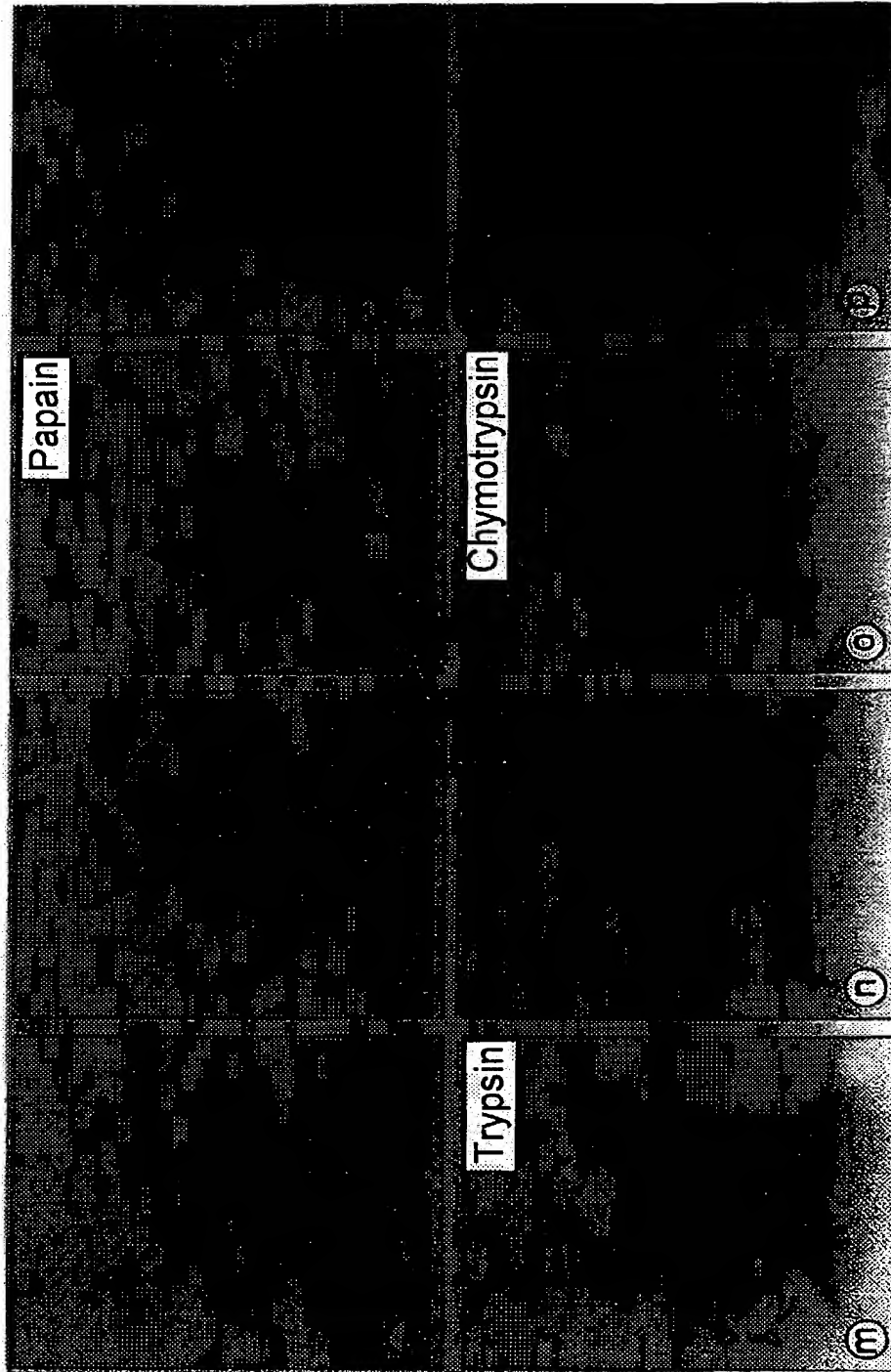
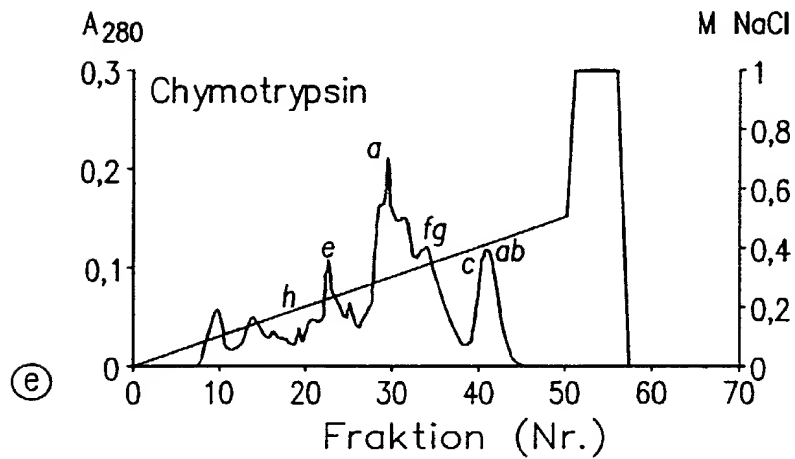
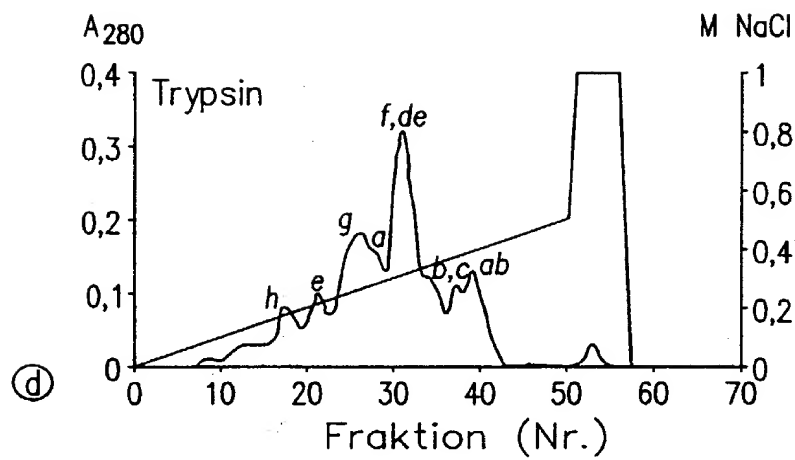


Fig. 2i-p



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Fig. 3d-e



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Figur 4

cDNA-Sequenz in Verbindung mit Intronstruktur des HtH1

Domäne a

GGCTTGTTTCAGTTTCTACTCGTCGCCCTTGTGGCGGGGGCTGGAGCAGACAACGTCGTCAG
AAGGAGCGTGAAGTCACCTCACGGATGACGAGGTGCAAGCTCTCCACGGCGCCCTCCRTGAC
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CGTCGTGTGACTACAAGGGACGGAAGATCGCCTGCTGTGTCCACGGTATGCCAGTTTCCC
CTTCTGGGCACAGGGCATATGTCTGCCAAGCCGAGCGGGCACTGTTGTCCAAACGGAAGACT
GTCCGGAATGCCCTTACTGGGACTGGACGCAACCGCTGACTCACTTACCATCTCTTGTGACTG
AACCCATCTACATTGACAGTAAAGGTGGAAAGGCTCAACCAACTACTGGTACCGGGCGGA
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CACCCTCCCAATGCAATGGACTGTGCACATGAACCTCGCTCACCAGCAACTCCALCCCTTCAA
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TACAAACAACCTTGGATACAGCTACGACAGCTTAAACCTGAATGGAAATGACGCCAGAACAGC
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AGTGATGACTACTGCGAGAAAGCAGGCGACTTCTTCATTCTTGGGGGTCALAGCGAAATGC
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TCACCTGATCTTCTTCCTCAACCAACTGTTGCCCTACCGACCTGGGAAAG

Domäne b

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Intron b/c

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TACCTATCTGCATAATGCAATACCCTGACTCCATATAAGTATAGTATATTTACTCTGGTCG
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GTCTGGACCAGACAATCGTGTGGAATGGTTTAGGCACATTATATCAAATTCATTGTTGAAG
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TGACTGAAATCTCTTCAACGCCGTTTAGCAATAATAGGCTCAGTAGTATTCAACCAATTAC
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ATTTTCTTTTCAG

Domäne c

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Intron c/d

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Domäne d

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Intron d/e

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Domäne e

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Intron e/f

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Domäne f

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Intron f(1)

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Domäne f(2)

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GATAATCTATGAACCAGGCGAAG

Intron f/g

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Domäne g(1)

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TCGCCTCTACACCAAGCAGATGGAGGATGCAATGAGGGCGCATGGGTCTCATGTGCGGCCTG
CCCTACTGGGACTGGACTGCTGCCTTCACCCACCTGCCAACACTGGTCACCGACACGGGACA
ACAACCCCTTCCAAACAT

Intron g(2)

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TGTATGTTCCGACTCACTGGTTGGTGCGTACCATTTCTACTGTACACTGAGAGGCCAATGTT
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AATGTAGTCAPACAGGTAACAATCTGTTAGTGAGCCCAGTTCGAGGTTGCGTTGTAGGGTG
TAGTCCAACAGGTAGGCAGTCCATAGCATAGTTTTTAAGCATTTTTAGATCATCTATAATT
AACCACATGGTTAGCCGCTATGTTTAGTTTAATCCAGTATAGTTAGAACTGTTATATTTTC
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Domäne g(2)

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GGCTTCACCACTCCAACACCCGACAGAATCTGGGCTGTCTGGCAAGCTTTGCLAGAATACAG
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GGAACCTTGATCGCGTGCTTGAAGAAAGAAAGGAGGAGGACAGAAATATTTGCTGCCTTCCTT
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Intron g/h

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Domäne h

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CCTTTCTCTTACCACGGCTTTGAACTGGACAAAGTCTACAGCGTCGATCACGGAGACTACT
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ACACGAGTAG

3' UTR

TTCACAG

Intron UTR

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3' UTR

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GACTTGGCGCTCTAGGACAAAGACATAATTCATCAGCACCCCTGTGCACCAACTCTTTGTTT
GCTGCAACGCTCTGACAAGCGACACGTCAATCAACAAGCTGTTCAAACCTCAAGTGGATGTA
ACTAGAATCGTTGGGGCCATCGTTCACAAAGTATTGACAGATGTCACACATGATGGCGAGAA
ACACTTTAGAATTTTAAATGACCTAGAGTGACTTGTAATATGTAATATATTTCTTCAAAG
ACTCAGCTGAACATATTGTTGGATAACACATCAATCCCTCAACAAAATGCTTTATCTTCAC
ATGGATGTATGTAATGTGGCCGGCAATAAAGTATATATATGTATAAAAAAAAAAAAAAAAA
A

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Figur 5

Abgeleitete Primärstruktur des HtH1

Signalpeptid

LVQFLLVALVAGAGA

Domäne a

DNVVRKDVSHLTDDDEVQALHGALHDVTASTGPLSFEDITSYHAAPASCDYKGRKIAACCVHG
MPSPFPWHRAYVVQAEALLSKRKTVMGMPYWDWTQTLTHLPSLVTEPIYIDSKGGKAQNTY
WYRGEIAFINKKTARAVDDRLFEKVEPGHYTHLMTVLDALQDEFCKFETIQFELAHNAIH
YLVGGKFEYSMSNLEYTSYDPIFFLHRSNVDRLFATWQRLQELRGKNPNAMDCAHSLAHQQ
LQPFNRDSNPVQLTKDHSTPADLFDYKQLGYSYDSLNLNGMTPEQLKTELDERHRSKERAFA
SFRLSGFGGSANVVVYACVPDDDDPRSDDYCEKAGDFFILGGQSEMPWRFPYRPTFFYDVTEAV
HHLGVPLSGHYVVKTELFVNGTALSPDLLPQPTVAYRPGK

Domäne b

GHLDPVVEHRHDDDLIVRKNI DHLTREEEYELRMALERFOADTSVDGYQATVEYHGLPARC
PRPDAKVRFAACCMHGMAFPHWHRLFVTQVEDALVRRGSPIGVPYWDWTKPMTHLPDLASN
ETVVDPYGHTHNPFFNANISFEEGGHHTSRMIDSKLFAPVAFGEHSHLFDGILYAFEQED
FCDFEIQFELVHNSIHAWIGGSEDDYSMATLHYTAFDPIFYLHHSNVDRLWAIWQALQIRRH
KPYQAHCAQSVEQLPMKPFAPPSPLNNEKTHSHSVPTDIYDYEEVLHYSYDDLTFGGMNL
EEIEBAIHLRQQHERVFAGFLLAGIGTSALVDIFINKPGNQPLKAGDIALGGAKEMPWAF
DRLYKVEITDSLKTLSLDVDGDYEVTFKIHDMHGNAIDTDLI PHAAVVSEPAH

Domäne c

PTFEDEKHS LRIRKNVDSLTP EETNELRKALELLENDHTAGGFNQLGAFHGEPKWCPNPEA
EHKVACCVHGMVFPWHRLALQAEALRKHGYS GALPYWDWTRPLSOLPDLVSHEQYTD
PSDHHVKHNPWFNGHIDTVNQD TTRSVDRELYQQPEFGHFTDIAQOVLLALEQDDFCSEV
QYEISHNFIALVGGT DAYGMA SLRYTAYDPIFFLHHSNTDRIWAIWQSLQYRGKPYNTA
NCAIESMRRPLQPFGLSSAINPDRI TREHAIPFDVFNRYRDNLHYVYDTLEFNGLSISQLDR
ELEKIKSHERVFAGFLLSGIKKSALVKFEVCTPPDNCHKAGEFYLLGDENEMAWAYDRLEK
YDITQVLEANHLHFYDHLFIRYEVFDLKGVS LGTDLFHTANVVHDSGT

Domäne d

GTRDRDNYVEEVTGASHIRKNLNDLNTGEMESLRAAFLHIQDDGTYESIAQYHGKPGKCQL
NDHNIACCVHGMPTFPQWHRLYVVQVENALLNRGSGVAVPYWEWTAPIDHLPHFIDDATYF
NSRQORYDPNPFFRGKVT FENAVTTRDPQAGLPNSDYMYENVLLALEQENYCDFETIQFELV
HNALHSM LGGKGQYSMS SLDYSAFDPVFFLHHANTDRLWAIWQELQRFREL PYEEANCAN
LMHQP LKPFSDPHENHDNVT LKYSKPODGF DYQNHFGYKYDNLEFHLSIPSLDATLKQRR
NHDRVFAGFLLHNIGTSADITIYICLPDGRRGNDCSHEAGTFYILGGGETEMPFIIDRLYKF
EITKPLQQLGVKLHGGVFELBLEIKAYNGSYLDPHTFDPTIIFEPGT

Domäne e

VHRRGNGHEDEHHDDRDLADVLIRKEVDFLSLQEANAKDALYKLQNDSSKGGFEAIAGYHGY
PNMCPERGTDKYPCCVHGMVPVFPHWRRLHTIQMERALKNHGSPMGIPYWDWTKKMSSSPSF
FGDSSNNMNPYKYVIRGVQHETTRDVNQRLFNQTKFGEFDYLYYLTQLQVLENSYCDFEQ
YEILHNAVHWSLGGTGQYSMSTLEYSAFDPVFMIIHSSLDRIWILWQKLQKIRMKPYVALD
CAGDRLMKDPLHPFNYETVNEDEFTRINSFPSILFDHYRFNYEYDNMIRGQDIHELEEV
QELRNKDRI FAGFVLSGLRISATVKVFIHSHKNDTSHEEYAGEFAVLGGGEKEMPWAYERMLK
LDISDAVHKLHVKDEDIRFVVVYATYNGDVVTRLSQPFIVHRPAHVAHDILVIVPGAGHD
LPPKVVVKSGLKVEFTPIDSSVNKAMVELGSYTAMAKCIVPPFSYHGFE LDKVYSVDHGDY
YIAAGTHALCEONRLRHHVHEH

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Figur 6

cDNA-Sequenz in Verbindung mit Intronstruktur des HtH2

Domäne b

CACAGACTGTTGCTCAGCCAGGTGGAAGATGCTCTGATCAGGCGAGGATCGCCTATAGGGG
 TCCCTACTGGGACTGGACTCAGCCTATGGCGCATCTCCAGGACTTGCAGACAACGCCAC
 CTATAGAGATCCCATCAGCGGGGACAGCAGACACAACCCCTTCCAGCATGTTGAAGTTGCC
 TTTGAAATGGACGTACAGAACGTCACCCAGATAGTAGATTGTTTGAAACACCTTTATTG
 GCALACATACGCGTCTCTTCGACAGTATAGTCTATGCTTTTGAGCAGGAGGACTTCTGGA
 TTTTGAAAGTTCAATTTGAGATGACCCATAATATATTCACGCCTGGATTGGTGGCGGGCAG
 AAGTATTCATGTCTCTCTACACTACACAGCCTTCGACCCCTATCTTCTACCTTCGTCAC
 CCAACACTGACCGGCTCTGGGCAATTTGGCAAGCGTTGCAGATACGAAGAACAGGCCTTA
 CAAGGCTCATTTGTGCTTGGTCTGAGGAACGCCAGCCTCTCAAACCTTTGCGCTTCAGTTCC
 CCACTGAACACCAACGAACCAACCTACGAAACCTCGGTGCCACCAACGTTTACGACTACG
 AAGGAGTCCTTGGCTATACTTATGATGACCTCAACTTCGGGGGCATGGACCTGGGTACGCT
 TGAGGAATACATCCAGAGGCAGAGACAGAGAGACAGGACCTTTGCTGGTTTCTTTCTGTCA
 CATATTGGTACATCAGCGAATGTTGAAATCATTTATAGACCATGGGACTCTTCATACCTCCG
 TGGGCACGTTTGGCTGTTCTTGGCGGAGAGAAAGGAGATGAAATGGGGATTTGACCGTTTGT
 CAAATATGAGATTACAGATGAACGAGGCAACTTAATCTCCGTGCTGATGATGTTTTTCAGC
 ATCTCTGTTAAAGTAACTGATGTTGATGGCAGTGAGCTGTCTCTGAACTCATCCCATCTG
 CTGCTATCATCTTCGAACGAAGCCATA

Intron b/c

GTAAGTAGCTACCTGTTTATTCAATTTTTTCGCTTTGCCAATCAATTCATTCAGCTTGAAA
 TTCAATAAATTGTGTTTTGCATGGCTGAAACCAATTTGAACTCTTTTCTTTCTCAGGTGC
 AACTCAAATAAATAATCACTAATTGTTATGCACGCGGGTAGGGCATACATACTATATCCAC
 ATCGGTATCTCAATAATGCAACAAATTTGTCTTATTTCCGTTGGGACAAAGCAACCCCTT
 TCCTGTAATCTTGCCTTTGGCATCCACTGGAATTAATGTTGACTGGTAATTGATACTGGCT
 CTCTTCTTGCATAGAGTTAATATCTATAGTTTGTAAATCTTTATGATTTTGCTATTTATAT
 TTGACAGCATGCTATAGACACCCTAGACTATTGTATAGCCACTTGTATTGTTTTTCCATT
 TATTATTTATAACAGAACATGGCTTGTAATTTTTTATTTACCTTCCAG

Domäne c

TTGACCATCAGGACCCGCGATCATGACACAATCATTAGGAAAAATGTTGATAATCTTACACC
 CGAGGAAATTAATTCTCTGAGGCGGGCAATGGCAGACCTTCAATCAGACAAACCGCCGCT
 GGATTCCAGCAAAATTGCTGCTTTTCACGGGGAAACCCAAATGGTGCCCAAGTCCCGATGCTG
 AGAAGAAGTTCTCTGCTGTGTCCATGGAATGGCTGTCTTCCCTCACTGGCACAGACTCCT
 GACCGTGCAAGGCGAGAATGCCCTGAGAAAGCATGGATGTCTCGGAGCTCTCCCTACTGG
 GACTGGACTCGGCCCTGTCTCACCTACCTGATTTGGTTTTGGTAAGTAGCAGAACTACAC
 CGATGCCATATTCCACCGTGGAAGCCCGAAACCCCTGGTACAGCGGCCATATTGATACAGT
 TGGTGTGACACACAAAGAAGCGTCCGTCAAGAAGTGTATGAAGCTCCTGGATTGTGCCAT
 TATACTGGGGTGGCTAAGCAAGTGCTTCTGGCTTTGGAGCAGGATGACTTCTGTGATTTTG
 AAGTCCAGTTTGAGATAGCTCACAAATTCATTCACGCTCTTGTGGCGGGAAGCGAGCCATA
 TGGTATGGCGTCACTCCGTTACACTACTTATGATCCAATTTTCTACCTCCATCATTTCTAAC
 ACTGCAGAGACTCTGGGCTATATGGCAGGCTCTACAAAAGTACAGGGGCAAACCTTACAATT
 CGGCCAATGCGCCATTGCTTCTATGAGAAAACCCCTACAACCCTTTGGTCTGACTGATGA
 GATCAACCCGGATGATGAGACAAGACAGCATGTCTTCTTCCAGTGCTCTTGATTCAAG
 AACAACTTCAATTATGAATATGACACCCTTGACTTCAACGGACTATCAATCTCCAGCTGG
 ACCGTGAACTGTCACGGAGAAAGTCTCATGACAGAGTATTTGCCGGATTTTGTGCTGCATGG

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TATTCAGCAGTCTGCACTAGTTAAATTCTTTGTCTGCAAATCAGATGATGACTGTGACCAC
 TATGCTGGTGAATTCTACATCCTTGGTGATGAAGCTGAAATGCCATGGGGCTATGATCGTC
 TTTACAAATATGAGATCACTGAGCAGCTCAATGCCCTGGATCTACACATCGGAGATAGATT
 CTTTCATCAGATACGAAGCGTTTGATCTTCATGGTACAAGTCTTGGAAGCAACATCTTCCCC
 AACCTTCTGTCTATACATGACGAAGGGGACG

Intron c/d

GTGAGAACATTGATAATAGTTCAAATGAAGTATATCCGATTCAAGCTGTGCGATACAAGATG
 AGATACATAATCACAATGTTTGTATTAGATATCTCTCTTAATTTAATGCCGCTTTTATCAA
 TATTCGAGCAATCCTTCAGCAACATACACCAGCAATGTTTCATCAACAGACTATATTATT
 TAATCTTTTAAAAATCCTTTTCTGTTGTTATAAATACTTAAAGTATCGAATTCCTTGAAATG
 CGTCTTCTCTGCAAGCATATAGTTAAGTTGTTGTGTTTCTCTGTCTAG

Domäne d

GTCACCATCAGGCTGACGAGTACGACGAAGTTGTAAGTCTGCTGCAAGCCACATCAGAAAGAA
 TTTAAAGATCTGTCAAAGGGAGAAGTAGAGAGCCTAAGGTCTGCCTTCCTGCAACTTCAG
 AACGACGGAGTCTATGAGAATATTGCCAAGTTCCACGGCAAGCCTGGGTTGTGTGATGATA
 ACGGTGCGAAGGTTGCCTGTTGTGTCCATGGAATGCCACCTTCCCCCAGTGGCACAGGCT
 CTATGTCCTCCAGGTGGAGAATGCTTTGCTGGAGAGAGGATCTGCCGTCTCTGTSCCATAC
 TGGGACTGGACTGAAACATTTACAGAGCTGCCATCTTTGATTGCTGAGGCTACCTATTTCA
 ATTCCCGTCAACAAACGTTTGACCCTAATCCTTTCTTCAGAGGTAAATCAGTTTGTGAAA
 TGCTGTTACAACACGTGATCCCCAGCCTGAGCTGTACGTTAACAGGTACTACTACCAAAC
 GTCATGTTGGTTTTTGAACAGGACAACACTACTGCGACTTCGAGATACAGTTTGAGATGGTTC
 ACAATGTTCTCCATGCTTGGCTTGGTGGAGAGCTACTTATTCTATTTCTTCTCTTGATTA
 TTCTGCATTGCAACCTGTGTTTTCTTCCATGCGAACACAGATAGATTGTGGGCCATC
 TGGCAGGAGCTGCAGAGGTACAGGAAGAAGCCATACAATGAAGCGGATTGTGCCATTAACC
 TAATGCGCAAACCTCTACATCCCTTCGACAACAGTGATCTCAATCATGATCCTGTAACCTT
 TAAATACTCAAAACCCACTGATGGCTTTGACTACCAGAACAACCTTTGGATACAAGTATGAC
 AACCTTGAGTTCAATCATTTTCAGTATTCCGAGGCTTGAAGAAATCATTGCTATTAGACAAC
 GTCAAGATCGTGTGTTTGCAGGATTCCCTCCTTCACAACATTGGGACATCCGCAACTTTGA
 GATATTCGTCTGTGTCCTTACCACAGCGGTGAGCAAACTGTGAAAACAAAGCCGGAACA
 TTTGCCGTACTCGGAGGAGAAACAGAGATGGCGTTTCATTTTGACAGACTCTACAGGTTTG
 ACATCAGTGAAACACTGAGGGACCTCGGCATACAGCTGGACAGCCATGACTTTGACCTCAG
 CATCAAGATTCAAGGAGTAAATGGATCCTACCTTGATCCACACATCCTGCCAGAGCCATCC
 TTGATTTTTGTGCCTGGTTCAAGT

Intron d/e

AAGAAAGTTTCACTGTCTAAATCTTTTTTTATGATAGAGGGTAGAGAAGTGGAGACAATGT
 GACAATATATTGAATAAAGTTGTTTAAATTTATAACTCTCATAAGTTCATATTATGCTGA
 AGCTGTAGCCATCTATAACTGTGTAACATGAAATGTTAAGACATTAACCTAATACTTCAG
 CTGATAACAAAACAATGTTAATACATACGTCAATGTAACATTTCTTATCTTTAGGTTATA
 GCATAAACACTTCAGAGATACAGTGACGAAAACCTCTATTTAAATATTTTCAGGT

Domäne e

TCTTTCCCTGCGTCTGATGGGCATTTCAGATGACATCCTTGTGAGAAAAGAAGTGAACAGCC
 TGACAACCAGGGAGACTGCATCTCTGATCCATGCTCTGAAAAGTATGCAGGAAGACCATTC
 ACCTGACGGGTTCCAAGCCATTGCCTCTTTCCATGCTCTGCCACCACTCTGCCCTTCACCA
 TCTGCAAGCTCACCGTTATGCTTGTGTGTCACGGCATGGCTACATTTCCCCAGTGGCACA
 GATTGTACACTGTACAGTTCCAGGATGCACTGAGGAGACATGGAGCTACGGTAGGTGTACC
 GTATTGGGATTGGCTGCGACCGCAGTCTCACCTACCAGAGCTTGTCAACCATGGAGACATAC

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CATGATATTTGGAGTAACAGAGATTTCCCCAATCCTTTCTACCAAGCCAAATATTGAGTTTG
AAGGAGAAACATTACAACAGAGAGAGAGAGTCAATTGCAGACAAACTTTTTGTCAAAGGTGG
ACACGTTTTTGTATAAACTGGTTCTTCAAACAAGCCATCCTAGCGCTGAGCAGGAAAACCTAC
TGTGACTTTGAGATTCAAGTTTGAAATTCTTCAACAACGGCGTTACACAGTGGGTGGGAGGCA
GTCGTACCTACTCTATCGGACATCTTCATTACGCATTCTACGACCCTCTTTTCTACCTTCA
CCATTTCCAGACAGACCGTATTTGGGCAATCTGGCAAGAACTCCAGGAACAGAGAGGGGCTC
TCGGGTGATGAGGCTCACTGTGCTCTCGAGCAATGAGAGAACCATTGAAGCCTTTCAAGCT
TCGGCGCTCCTTATAACTGGAATCAGCTCACACAGGATTTCTCCCGACCCGAGGACACCTT
CGACTACAGGAAGTTTGGTTATGATATGACAATTTAGAAATTCCTGGGAAATGTCAGTTGCT
GAACTGGATCAATACATTATTGAACATCAAGAAAATGATAGAGTATTCGCTGGGTTCTCTGT
TGAGTGGATTCCGAGGTTCCGCATCAGTTAATTTCCAGGTTTGTAGAGCTGATTCCACATG
TCAGGATGCTGGGTACTTCACCGTTCTTGGTGGCAGTGTGAGATGGCGTGGGCATTTGAC
AGGCTTTACAAATATGACATTACTGAAACTCTGGAGAAAATGCACCTTCGATATGATGATG
ACTTCACAAATCTCTGTCACTCTGACCGCCAAACAACGGAATGTCTCTGAGCAGCAGTCTAAT
CCCAACACCCGAGTGTCAATTTCCAGCGGGGACATC

Intron e/f

AAGTAGTAAACTGCTCAGATTGTTTTTCATAATTACTCCACTATTAAGTAAAAAGTACTAGT
AATTCAATAGTACTGTTCCACAGAGAAATGTAACACAATAGACCACAGAGTCCATTTGTTAA
ACGCTTTTGGCTTGGTAAGTCTGAGGTTTTTGGTGACTGATGGAAGCTAATATATATTTTG
ACAG

Domäne f(1)

GTGACATAAATACCAGGAGCATGTCACCGAACCGTGTTCCCGGTGAGCTGAGCGATCTGTC
TGCGAGGGACCTGTCTAGTCTCAAGTCTGCTCTGCGAGACCTACAGGAGGATGATGGCCCC
AACGGATACCAGGCTCTTGACAGCCTTCCATGGGCTACCAGCAGGCTGCCATGATAGCCGGG
GAAATGAGAT

Intron f

ATATTTAAAGTATTTTATCTTACGCATGACCCCTGACCCCTATTATTTTTTTPATCCTATGAT
GAAACATTTACTTAGACTGGCTTGTGAGCCCCAGGCAAAATGCACTGTAAAAATACACTGA
CAGAGGATTAGGCATTCTTGGGAGTACTGTATAGTTAGTTGCATACATATTAGCGTTCCCT
CACTAAAACGAATCTCTGAATGCTATCAATTAAAGATCATGATGCTTTGATTGTGTCTACT
GTATTTAAATGTTGTTAAGATTTGCAATTACAATATACACAACACGTTTCTGCACTCTC
GGAGAATGCAATCTTTTCGTTGTACGCGTCTGTTTTATATTTTATGCACTGTAGTTTGCAC
TACTTAGCGTCCAAATAAATCCATTACAAAATCACACAAACAAACGATTTTAGGAATGTGA
CTGTAGCTGCAACGAATATACCTGATCCTTTCTTGTTCAGAT

Domäne f(2)

CGCATGTTGCATTACAGGGATGCCGACCTTCCCCAGTGGCACAGACTGTACACCCTGCAG
TTGGAGATGGCTCTGAGGAGACATGGATCATCTGTCCCATCCCCTACTGGGACTGGACAA
AGCCTATCTCCGAACCTCCCTCGCTCTTCAACAGCCCTGAGTATTATGACCCATGGCATGA
TGCTGTGGTAAACAAACCCATTCTCCAAAGGTTTTGTCAAATTTGCLAATACCTACACAGTA
AGAGACCCACAGGAGATGCTGTTCCAGCTTTGTGAACATGGAGAGTCAATCCTCTATGAGC
AACTCTTCTTGCTCTTGAGCAAACCGACTACTGTGATTTTGGAGGTACAGTTTGGAGTCTC
CCATAACGTGATCCACTACCTTGTGGTGGAGCTCAGACCTACGCATTGTCTTCTCTGCAT
TATGCCCTCCTACGACCCATTCTTCTTTATACACCATTCCTTTGTGGATAAGATGTGGGTAG
TATGGCAAGCTCTTCAAAGAGGAGGAACCTTCCATACAAAGCGAGCTGACTGTGCTGTCAA
CCTAATGACTAAACCAATGAGGCCATTTGACTCCGATATGAATCAGAACCCATTACAAAG
ATGCACGCAGTTCCCAACACACTCTATGACTCCGAGACACTGTACTACAGCTACGATAATC
TCGAAATAGGTGGCAGGAATCTCGACCAGCTTCAGGCTGAAATTGACAGAAGCAGAAGCCA

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CGATCGCGTTTTTGGCTGGATTCTTGCTTCGTGGAATCGGAACTTCTGCTGATGTCAGGTTT
 TGGATTTGTAGAAATGAAATGACTGCCACAGGGGTGGAATAATTTTCATCTTAGGTGGAG
 CCAAGGAAATGCCATGGTCATTTGACAGAACTTCAAGTTTGATATCACCCATGTACTCGA
 GAATGCTGGCATTAGCCCAGAGGACGTGTTTGATGCTGAGGAGCCATTTTATATCAAGGTT
 GAGATCCATGCTGTTAACAAGACCATGATACCGTCGTCTGTGATCCCAGCCCCAACTATCA
 TCTATTCTCCTGGGGAAG

Intron f/g

GTGAGAGAACCAGTAATAGCTACTGTCTACAAAGAATGTGTTTCATTTAAAGACCTGACTGT
 AGGCCGATGGCTGCTGTCTCTCCTCCGCTCCTCCTCCTGTTCCCTCCTCCGAAGGGGTCA
 GCTTCAGGTTCTCTTGCCAATATGCCAAGCAGACCTCCTGAGCAGGCAGTATATATACGTA
 AGGGAAAGCAAGTATGGACCATCGCGCGGCATGTAGAGATACAATGATCAGCTGTCTGCTGT
 TCCACTCCTGTGACACAATGAGATAAACATGAATACAGTATTACTCAGCAGCGTTTCCAATT
 TTTCAACCCTCGTATTTTATTAATAAAGGAATTTTAAATATATTTTCTCCTTGTGAAATA
 TTTTAGTAACGTGTTAATCGATATAGAGTGGAGTAGTGACGCTTTATTTTCGGTTCATTCTCG
 AAACAAAAATATAATAGTCCACTGAACTCTCTTAAATTGTTTTTACAACCTTCAACTGCCA
 CAGACGTAATCCCTCACGTTATTTTGAGCTGACAACGTGTTGAATTGAGTGTGTTCCGAAT
 TCTAATAAGCATGTATATATTTACGTCTCATGCAAGTAATATATGTTTTACTGATGACGT
 CACTTGGGTGACCACTGATTTAGTTCCTTTGTGATAATTGCAGTTTCTGTTGTACAGGGGAC
 GGTGGGGAAGCCAGGTTCCCTCCTGTGACGCTGAATATCCCGTTTGAATCCCCCACATGGGT
 ACAAGTGTGATGCCTATTTCTGGTGTCCCCACCGTGATATTGCTGGAATAAGTGGCTTA
 ATACCATATACACTCACTCTATTGTACACTACTGCCACCGGCTCACACCTCTGATGCTTC
 TGTTCATCCAG

Domäne g(1)

GTCGCGCTGCTGACAGTGCGCACTCTGCCAACATTGCTGGCTCTGGGGTGAGGAAGGACGT
 CACGACCCTCACTGTGTCTGAGACCGAGAACCTAAGACAGGCTCTTCAAGGTGTCTATCGAT
 GATACTGGTCCCAATGGTTACCAAGCAATAGCATCCTTCCACGGAAGTCCCTCCAATGTGCG
 AGATGAACGGCCGCAAGGTTGCCTGTTGTGCTCACG

Intron g(1)

GTAATTAATGGATGTGAAGTCAATGTCCGAGGGTATAATAAGGATTTAAATACTTCAGTCG
 TGTAATACTGTATGACATGTGTATTGGATGGTGTAGGTATTACAGGTTATAAGGCCAGTGT
 GTGTTGGGACGGTTACTTTCCCTGCACTAGTAATAAGCATTGTATTTAGCTAGCTTTTATCA
 TATAACTTTAGTTTCAGGTTTGCGCAATTGAAATCGAAATTTTCTTTTCAATTTCAAGGTTA
 TCGCACTCGTGTGTNAGAAATAGTTACTATGCTGCATTGAGAATAACACTATAGTAATAAAG
 CATATCATACAGTAAGAATAACACTATAGTAATAAAGTATATCATNCAGTAAGAATGTCAT
 TGTATGATAAATAGGTTATCACACTCGTGTGTTTTAGARTGGTTACTATCCCAGGAATAAC
 CACTATGTATTACATGTATATTGGGCAGTGTAAGTAGTAGCATTGTATATTAAATCAGTAT
 ATCGTGCTTCAAAACACCAGGATATATGGGGTATACAGTGGGCAGTGTAAGTAGCAACATT
 GTATATTAAATCAGTATATCGTACTTCAAAACACCAGGATTATGGGGTATACAGTGGGCAG
 TGTAAAGTAGTAGCATTGTATATTAAATCAGTATATCGTACTTCAAAACACCAGGATATAAT
 TCAGTATATCGTGCTTCAAAACACCAGGATATAATTCAGTATATCGTGCTTCAAAACACCA
 GGATATATGGGATATACAGTGCGGGTTTGCATACAACCTCCACCCTTTACAG

Domäne g(2)

GTATGGCCTCCTTCCACACTGGCACAGACTGTATGTGAAGCAGATGGAAGATGCCCTGGC
 TGACCACGGGTACATATCGGCATCCCTTACTGGGACTGGACAACCTGCCTTCACAGAGTTA
 CCGGCCCTTGTACAGACTCCGAGAACAAATCCCTTCCATGAG

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Intron g(2)

GTCAGTTT TAGTCTCCTGTCTGAGCTAACGATACCAATTTCTTATTTTCGAGAACCACGATG
 ACGAGAAAACAAGCAATATAGATATAGATGCAGTATAGATCAAGTTAATGAATTTCATTGCT
 ATATGTTTGCTTGTAAATAAACTTTAAGAAAACGAGAGCATGCACACAAATGAAACAAACAA
 TTATGTGTTTGATAGGAATATGATATATGTATTTGGGGGCTGACGTGAGCAGGGGTGAAGG
 GACAGTTTACATTGTCAGTAACACTGGGAGTATTCTTTGATCCACAATATATAGTTTCATT
 GTGTTACAGCAGTTACAACATAACATTATATCATACATTACGTCTGTAACATGCTTCTTTTGTG
 CTCTTTTGCCAG

Domäne g(3)

GGTCGCATTGATCATCTCGGTGTAACCACGTCACGTTCCCCCAGAGACATGCTGTTTAAAG
 ACCCAGAGCAAGGATCAGAGTCGTTCTTCTATAGACAAGTCCTCCTGGCTTTGGAGCAGAC
 TGACTACTGCCAGTTCGAAGTCCAGTTTGAGCTGACCCACAACGCCATTCACTCCTGGACA
 GGTGGACGTAGCCCTTACGGAATGTGACCCCTCGAGTTTCACAGCCTACGATCCTCTCTCT
 GGCTTCACCACTCCAACACCGACAGAACTCTGGGCTGTCTGGCAAGCACTGCAGAAATACCG
 AGGACTCCCATACAACGAAGCACACTGTGAATCCAGGTTCTGAACAGCCCTTGAGGCCA
 TTCAACGATGACATCAACCACAATCCAATCACCAGACTAATGCCAGGCCATATCGATTTCAT
 TTGATTATGAGAGCTTTAACTATCAGTATGACACCCTTAGCTTCCATGGTAAGAGCATCCC
 TGAACCTGAATGACCTGCTCGAGGAAAGAAAAGAGAAAGAGAGAACATTTGCTGCTTCTCT
 CTTGCTGGAAATCGGTTGCAGTGTCTGATGTCTCTTTGACATCTGCCGCCCCAATGGTGACT
 GTGTCTTTGCAGGAACCTTTGCTGTGCTGGGAGGGGAGCTAGAAATGCCCTTGGTCTCTCGA
 CAGACTGTTCCGCTATGACATCACCAGAGTCATGAATCAGCTCCATCTCCAGTATGATTCA
 GATTTTCAGTTTTCAGGGTGAAGCTTGTGTCACCAATGGCACTGAGCTTTTCATCAGACCTTC
 TCAAGTCACCAACAATTGAACATGAACCTTG

Intron g/h

GTATGTTATCTTATCATCAAATGTGTGATCAGATACTGGAGACGTTTTCATATTAACCTTGG
 TCAGCATTAGTTGATGATTTTGGTGCGATGTTGACGACAAGGAGTCAAGCATTAAACACATT
 CAACACATCTTTAATCTGATATGAGAAGGGAATAAATTGATCCAGTATTGATGATTGAAGT
 TAGATTAAACAGTGAAAGATATACCAGTTTTGATAATCGTATAAAACAGTAGCAGAATTGTA
 TCGTGAAAACATAAATGTGGGAAGGCGAACGCCAAGCAGATTTTAGATTACGATCGTGTGCT
 AGAATAATTCACAATAACCCAGACGTCGGAATGTGGTTGTCTATGGCAATGGTTACGATT
 AATTGCTAACATGCACGATTTACCTATTTCA

Domäne h

AGCCACAGAGGACCAGTTGAAGAAACAGAACTCACTCGCCAACATACTGACGGCAATGCA
 CACTTTTCATCGTAAGGAAGTTGATTCGCTGTCCCTGGATGAAGCAAACAACCTTGAAGAATG
 CCCTTTACAAGCTACAGAACGACCACAGTCTAACGGGATACGAAGCAATCTCTGGTTACCA
 TGGATACCCCAATCTGTGTCCGGAAGGAGCGATGACAAAATACCCCTGCTGCGTCCCCGG
 ATGGGCATCTTTTCCTTACTGGCACAGACTCTTGACCATTCAACTGGAAGAGCTCTTGAGC
 ACAATGGTGCAGTCTTGGTGTTCCTTACTGGGACTGGAACAAGGACCTGTCTGCTACTGCC
 GGCCTTCTTCTCCGACTCCAGCAACAACCAATCCCTACTTCAAGTACCACATCGCCGGTGT
 GGTCAAGACACCGTCAGAGAGCCAACTAGTCTTATATATAACCAGCCCCAAATCCATGGTT
 ATGATTATCTCTATTACCTAGCATTGACCACGCTTGAAGAAAACAATTACTGGGACTTTGA
 GGTTCAGTATGAGATCCTCCACAACGCCGTCCACTCCTGGCTTGGAGGATCCAGAAAGTAT
 TCCATGTCTACCCCTGGAGTATTCGGCCCTTTGACCCTGTCTTTATGATCCTTCACTCGGCTC
 TAGACAGACTTTGGATCATCTGGCAAGAACTTCAGAAAGATCAGGAGAAAGCCCTACAACCT
 CGCTAAATGTGCTTATCATATGATGGAGAGCCACTGGCGCCCTTCAGCTATCCATCTATC
 AACCAGGACGAGTTCACCCGTGCCAACTCCAAGCCTTCTACAGTTTTTTGACAGCCATAAGT

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TCGGCTACCATTACGATAACCTGAATGTTAGAGGTCACAGCATCCAAGAACTCAACACAAT
CATCAATGACTTGAGAAACACAGACAGAATCTACGCAGGATTTGTTTTGTCAGGCATCGGT
ACGCTCTGCTAGTGTCAAGATCTATCTCCGAACAGATGACAATGACGAAGAAGTTGGAACCTT
TCACTGTCCTGGGAGGAGAGAGGGGAAATGCCATGGGCCTACGAGCGAGTTTTCAAGTATGA
CATCACAGAGGTTGCAGATAGACTTAAAATTAAGTTATGGGGACACCCTTTAACTTCCGGA
ACTGGAGATCACATCCTTACGAATGGAATCGGTGGTAAACAAGAGCCTACCCAAATCCTTT
CATCATCTACAGACCTGCCAATCATGACTACGATGTTCTTGTTATCCCAAGTANGGAAGAAA
CCTTCACATCCCTCCCAAAGTTGTCTCAAGAAAGGCACCCGCATCGAGTTCCACCCAGTC
GATGATTCAGTTACGAGACCAAGTTGTTGATCTTGGAAGCTACACTGCACTCTTCAACTGTG
TGGTACCACCGTTTACATACCACGGATTGGAAGTGAACCACGTCTATTCTGTCAAGCCTGG
TGACTACTATGTTACTGGACCCACGAGAGACCTTTGCCAGAATGCAGATGTCAGGATTCAT
ATCCATGTTGAGGATGAGTAA

3' UTR

CGCAACAGGT

Intron UTR

GAGATAAGAAAACCCCTTCTAACAGTAATACGACACCACATTACAGCTTAAACATGATTGCCA
TCGATGTTTTTCATGTGTAGTATACGCTTTTCAGTTCTACATAATTTTTGTTTTTCAAATCAA
GTTTAGCAAATGAATCTATCACTGGAAAATAGGGTAGGGTAGCCAAGTGGTTAAAGCGGTG
ACTGATCACGCCAAAGACGAGTGTCTAACCTGCATGGGTACAAAAGTGAAGACCATTGCT
GGTGTCTACCGCCGTAATATTGTTTTTAGTATTGCTAAAACCTTATACTCACCCATGCGCTG
TAAAAGTGGAATAATAATCATATTTCAACAAAAGCACAAAACCATTTTCATTTTCATGAAAG
CCTCTTGTTTACCTGAAAGACGCAAGAGACAATAGTTTCTAACATTATTTTCAGACATTG
GAAATGTCCTGCACGTGTAAACCATATATCCTTTGAAATTTTTACGACTGCATCGTATACA
ATTTATGATATAAATTTAAACCTTTAT

3' UTR

TTCTTGGTCTCCACATATTCACATATCAGCACCAAATGGTTTTGGAAGGACATTGGCGTTCT
TCTCTGGCAATGCATTTCAATACAACATTGAAAATGACTTCAGCATATCAGTGTGCTTCGA
ACGTGTTCCGGAAGTACTCAAATGTGCTATGACTGAATTATTGTACATACATAACTTATTG
ATGTTCAATAAATAAATGTTGAAACGAAAAAAAAAAAAAAAAAAAAA

Figur 7

Abgeleitete Primärstruktur des HtH2

Domäne b

HRLFVTOVEDALIRRGSPIGVPYWDWTQPMALPGLADNATYRDPI SGDSRHNPFDHVEVA
FENGRTERHPDSRLFEQPLFGKHTRLFDSIVYAFEQEDFCDFEVQFEMTHNNIHA WIGGGE
KYSMSSLHYTAFDPIFYLRHSNTDRLWAIWQALQIRNRNPYKAHCAWSEERQPLKPFASFSS
PLNNNEKTYENSVPNTNVYDYEGVLGYTYDDLNFEGGMDLGQLEEYIQRQRQRDRTFAGFFLS
HIGTSANVEIIIDHGTLHTSVGTFVAVLGGEKEMKWGFDRLYKYEITDELRLNLNRADDVFS
ISVKVTDVDGSELSSSELIPSAAIIFERSH

Domäne c

IDHQDPHHDITIRKNVDNLTPEEINSLRRAMADLQSDKTAGGFQOIAAFHGE PKWCPSDA
EKKPSCCVHGMVFPWHRLTVQGENALRKHGCLGALPYWDWTRPLSHLPDLVLVSSRTT
PMPYSTVEARNPWYSGHIDTVGVDTTRSQRQELYEAPGFGHYTGVAQVLLALEQDDFCDF
EVQFEIAHNFIHALVGGSEPYGMASLRYTTYDPIFYLRHSNTDRLWAIWQALQYRGKPYN
SANCAIASMRKPLQPFGLTDEINPDDETROHAPFVSVDYKNNFNYYEYDTLDFNGLSISQL
DRELSRRKSHDRVFAGFLLHGIQQSALVKFFVCKSDDDCDHYAGEFYILGDEAEMPWGVDYR
LYKYEITEQLNALDLHIGDRFFIRYEAFDLHGTSLGSNIFPKPSVIHDEGA

Domäne d

GHHQADEYDEVVTAASHIRKNLKDLSKGEVESLRS AFLQLQNDGVYENIAKFHGKPGLCDD
NGRKVACCVHGMPTFPQWHRLYVLQVENALLERGS AVSVPYWDWTETFTELPSLIAEATYF
NSRQQTDFDPNPFGRKISFENAVTTRDPQPELYVNRYYYQNVMLVFEQDNYCDFEIQFEMV
HNVLHAWLGGRATYSSISLDYSAPDPVFFLHHANTDRLWAIWQELQRYRKPYNEADCAIN
LMRKPLHFPDNDLNHDPVTFKYSKPTDGFQYQNNFGYKYDNLEFNHFSIPRLESIIRIQ
RQDRVFAGFLLHNIQTSATVLIIFVCVPTTSGEQNCENKAGTEAVLGGETEMAFHFDRLYRF
DISETLRDLGIQLDSHDFDLSIKIQGVNGSYLDPHILPEPSLIIFVPGSS

Domäne e

SFLRPDGHSDDILVRKEVNSLTRETASLIHALKSMQEDHSPDGFQAIASFHALPPLCPSP
SAAHRYACCVHGMATFPQWHRLYTVQFQDALRRHGATVGVYWDWLRPQSHLPPELVMTETY
HDIWSNRDFPNPFYQANIEFEGENIT TEREVIADKLFVKGGHVFDKLVLTQTSHPSAEQENY
CDFEIQFEILHNGVHTWVGGSRTYSIGHLHYAFYDPLFYLRHHTQTDRIWAIWQELQEQGL
SGDEAHCALEQMREPLKPFSGAPYNWNQLTQDFSRPEDTFDYRKFGYEYDNLEFLGMSVA
ELDQYIIIEHQENDRVFAGFLLSGFGGSASVNFQVCRADSTCQDAGYFTVLGGS AEMAWAFD
RLYKYDITETLEKMLRYDDDFITISVSLTANNGTVLSSSLIPTPSVIFORGH

Domäne f

RDINTRSMSPNRVRRELSDL SARDLSSLSKALRDLOEDDGPNQYQALAAFHGLPAGCHDSR
GNEIACCIHGMPTFPQWHRLYTLQLEMALRRHGSSVAIPYWDWTKPISELPSLFTSPEYYD
PWHDAVVNNPFSKGFVKFANTYTVRDPQEMLFQLCENGESILYEQTLLALEQTDYCDFEVQ
FEVLHNVIIHYLVGGROTALSSSLHYASYDFFFFIHHSFVDKMWVWQALQKRRLPYKRA
CAVNLMTKPMRPFSDMNQNPFTKMHAVPNTLYDYETLYSSYDNLEIGGRNL DQLQAEIDR

GAHRGPVEETEVTQRQHTDGNNAHFHRKEVDSLSLDEANNLKNALYKLQNDHSLTGYEATISGY
HGYPNLCPEEGDDKIPLLRPRMGIFPYWHRLLTIQLERALEHNGALLGVPYWDWNKDLSSL
PAFFSDSSNNNPYFKYHIAGVGHDVTREPTSLIYNQPQIHGYDYLTYLALTLENNYWDF
EVQYEILHNAVHWSLGGSSQKYSMSTLEYSAFDPVFEMILHSGLDRLWI IWQELQKIRRKPN
FAKCAHYHMEEPLAPFSYPSINQDEFTRANSPSTVFDHSHKFGYHYDNLNVRGHSIQELNT
IINDLRNTDRIYAGFVLSGIGTSASVKIYLRTDDNDEEVGTFTVLGGGEREMPWAYERVFKY
DITEVDARLKIKLWGHPLTSGTGDHILTNIGIGGKQEPQTILSSSTDLPIMTTMFLLSQXGR
NLHIIPPKVVVKKGTRIEFHPVDDSVTRPVVDLGSYALFNCCVVPFPTYHGFELNHVYSVKP
GDYYVTGPTRDLCONADVRIHIHVEDE

Figur 8

cDNA-Sequenz in Verbindung mit Intronstruktur des KLH1

Domäne b

GGCCTACCGTACTGGGACTGGACTGAACCCATGACACACATTCCGGGTCTGGCAGGAAACA
 AACTTTATGTGGATTCTCATGGTGCATCCCACACAAATCCTTTTCATAGTTCAGTGATTGC
 ATTTGAAGAAAATGCTCCCCACACCAAAAGACAAATAGATCAAAGACTCTTTAAACCCGCT
 ACCTTTGGACACCACACAGACCTGTTCAACCAGATTTTGTATGCCTTTGAACAAGAAGATT
 ACTGTGACTTTGAAGTCCAATTTGAGATTACCCATAACACGATTTCACGCTTGGACAGGAGG
 AAGCGAACATTTCTCAATGTGCTCCCTACATTACACAGCTTTGATCCTTTGTTTACTTT
 CACCATTCTAACGTTGATCGTCTTTGGGCGCTTTGGCAAGCCTTACAGATGAGACGGCATA
 AACCTACAGGGCCCACTGCGCCATATCTCTGGAACATATGCATCTGAAACCATTGCGCTT
 TTCATCTCCCTTAACAATAACGAAAGACTCATGCCAATGCCATGCCAAACAAGATCTAC
 GACTATGAAAATGTCTCCATTACACATACGAAGATTTAACATTTGGAGGCATCTCTCTGG
 AAAACATAGAAAAGATGATCCACGAAAACCAGCAAGAAGACAGAATATATGCCGGTTTTCT
 CCTGGCTGGCATACTGACTTCAGCAAATGTTGATATCTTCATTAAAACTACCGATTCCGTG
 CAACATAAGGCTGGAACATTTGCAGTGCTCGGTGGAAGCAAGGAAATGAAGTGGGGATTTG
 ATCGCGTTTTTCAAGTTTGACATCACGCACGTTTTTGAAGATCTCGATCTCACTGCTGATGG
 CGATTTTCGAAGTTACTGTTGACATCACTGAAGTCGATGGAACCTAACTTGCATCCAGTCTT
 ATCCACATGCTTCTGTCTTCGTGAGCATGCACGTGGTAAGCTGAATAGAG

Intron b/c

GTTTTGTAATAATTATGTAGAATTCTTTACCTCAGAATAAGATGAGGTCACATGGGTTTTG
 CAAAACATTACGTTGPAATTAATATTAATAATACCGGACCCCTCCACTGGTACATATTTAT
 CTTTATAACGATAATAGCGATGATGATGATGATGATGATGATGATGATGATGATGATAATG
 ATGATGCCGGTATTGCACGTAATCCAGCCGACTTAGATGACACCCTAAGGGTGCAGAAAGT
 ATAACAATTAGATTGCGTTTGCATCTGTGTATGCGTGTGCTTTAAACCAAAAGTCAAAATAA
 AAGTGCAAAACCCTTAGTTTATTTCATTTGATAGAGCCCTTTTACGATAAGAACAATGTAATAA
 ATTAGAACATAACTGAAACCTCCGAAAGAAGGCCTGTTTGTCAAGAGAGGTATCGACATGA
 TTGACTTATAAACCTGTGCTTCTATATTTTGGAACTGTCCACTTTCTTGTGTGTGTA
 TAATCACATCGCACTATGGCTGCAAGACGTGTACGAGTACACTATATACTTACCTAATGAC
 CAACCACAAGGCTGGCTTTGTTAATATTTGTTATTTTACAGAAATAAACACAGAATTCCAGC
 ATTTGGCTGGTGTATTTAGCAAAACACCGATATGACACTCATGTTTTATTACATTTTTTTT
 AG

Domäne c

TTAAATTTGACAAAGTGCCAAAGGAGTCTGCTTATTTCGAAAAATGTAGACCGTTTGAGCCC
 CGAGGAGATGAATGAACCTTCGTAAAGCCCTAGCCTTACTGAAAGAGGACAAAAGTGCCGGT
 GGATTTTCAGCAGCTTGGTGCATTCCATGGGGAGCCAAAATGGTGTCTAGTCCCGAAGCAT
 CTAAAAAATTTGCCTGCTGTGTTACCGCATGTCTGTGTTCCCTCACTGGCATCGACTGTT
 GACGGTTTCAGAGTGAAAATGCTTTGAGACGACATGGCTACGATGGAGCTTTGCCGTACTGG
 GATTGGACCTCTCCTCTTAATCACTTCCCGAAGTGGCAGATCATGAGAAGTACGTCGACC
 CTGAAGATGGGGTAGAGAAGCATAACCCCTGGTTGATGGTCATATAGATACAGTCGACAA
 AACAAACAAGAAGTGTTCAGAAATAACTCTTCGAACAGCCTGAGTTTGGTCATTATACA
 AGCATTGCCAAACAAGTACTGCTAGCGTTGGAACAGGACAATTTCTGTGACTTTGAAATCC
 AATATGAGATTGCCCATAACTACATCCATGCACTTGTAGGAGGCGCTCAGCCTTATGGTAT
 GGCATCGCTTCGCTACACTGCTTTTGTATCCACTATTCTACTTGCATCACTCTAATACAGAT
 CGTATATGGGCAATATGGCAGGCTTTACAGAAGTACAGAGGAAAACCGTACAACGTTGCTA
 ACTGTGCTGTTACATCGATGAGAGAACCTTTGCAACCATTTGGCCTCTCTGCCAATATCAA
 CACAGACCATGTAACCAAGGAGCATTCAGTGCCATTCAACGTTTTTGTATTACAAGACCAAT

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TTCAATTATGAATATGACACTTTGGAATTTAACGGTCTCTCAATCTCTCAGTTGAATAAAA
AGCTCGAAGCGATAAAGAGCCAAGACAGCTTCTTTGCAGGCTTCCTGTTATCTGGTTTCAA
GAAATCATCTCTTGTTAAATTCAATATTTGCACCGATAGCAGCAACTGTCACCCCGCTGGA
GAGTTTTTACCTTCTGGGTGATGAAAACGAGATGCCATGGGCATACGATAGAGTCTTCAAT
ATGACATAACCGAAAACTCCACGATCTAAAGCTGCATGCAGAAGACCACTTCTACATTGA
CTATGAAGTATTTGACCTTAAACCAGCAAGCCTGGGAAAAGATTTGTTCAAGCAGCCTTCA
GTCATTTCATGAACCAAGAATAG

Intron c/d

GTACTTGTTATATGTTTCGAATATTGCCGATACCTTCAATATATATACTTTATCAAAGTAA
TTGATTAATCTGAAGTAATTTTCCCTTCCAGTAGAGATTGAGTTGATACAACAAGAATTGCG
CCCTGTTGTATGTCACCTTATTTTCATCAAACGATTGGAAGTGAGCTGTCCATGCCACAA
GGGGTCTCTGTAACCTTCTCGTATGGGGTATAGATTATATAGACGTGGCAGACCTTACGTA
TAACTAATATTTGTGTAATGTGCTTTCAG

Domäne d

GTCACCATGAAGGCGAAGTATATCAAGCTGAAGTAACTTCTGCCAACCGTATTGCAAAAAA
CATTGAAAATCTGAGCCTTGGTGAAGTCTGAGAGCTGCCTTCCTGGAAATTGAA
AACGATGGAACTTACGAATCAATAGCTAAATTCCATGGTAGCCCTGGTTTGTGCCAGTTAA
ATGGTAACCCCATCTCTTGTTGTGTCATGGCATGCCAACTTTCCCTCACTGGCACAGACT
GTACGTGGTTGTGCTTGAGAATGCCCTCCTGAAAAAAGGATCATCTGTAGCTGTTCCCTAT
TGGGACTGGACAAAACGAATCGAACATTTACCTCACCTGATTTTCAGACGCCACTTACTACA
ATTCCAGGCAACATCACTATGAGACAAAACCCATTCCATCATGGCAAAATCACACACGAGAA
TGAAACTCACTACTAGGGATCCCAAGGACAGCCTCTTCCATTGAGACTACTTTTACGAGCAG
GTCCTTTACGCCCTTGGAGCAGGATAAATTCTGTGATTTTCGAGATTGAGTTGGAGATATTAC
ACAATGCATTGCATTCTTTACTTGGTGGCAAAGGTAAATATTCCATGTCAAACCTTGATTA
CGCTGCTTTTGTATCCTGTGTTCTTCTTCATCACGCAACGACTGACAGAATCTGGGCAATC
TGGCAAGACCTTCAGAGGTTCCGAAAACGGCCATACCGAGAAGCGAATTGCGCTATCCAAT
TGATGCACACGCCACTCCAGCCGTTTGATAAGAGCGACAACAATGACGAGGCAACGAAAAC
GCATGCCACTCCACATGATGTTTTGAATATCAAACAGCTTTGGTTATGCTTACGATAAT
CTGGAACCTGAATCACTACTCGATTCCCTCAGCTTGATCACATGCTGCPAGAAAGAAAAGGC
ATGACAGAGTATTCGCTGGCTTCCTCCCTCACAAATATTGGAACATCTGCCGATGGCCATGT
ATTTGTATGTCTCCCAACTGGGGAACACACGAAGGACTGCAGTCATGAGGCTGGTATGTTT
TCCATCTTAGGCGGTCAAACGGAGATGTCCCTTTGTATTTGACAGACTTTACAACTTGACA
TAACTAAAGCCTTGAAAAAGAACGGGTGTGCACCTGCAAGGGGATTTGATCTGGAAATTGA
GATTACGGCTGTGAATGGATCTCATCTAGACAGTCATGTCATCCACTCTCCCACTATACTG
TTTGAGGGCCGGAACAG

Intron d/e

GTAATATTTTGTCACTGTAACCAACAACCTGCAGTCTATTTTGCAATTACGATAATAACAA
TTTTTGAATATATCTTTATTAPAGCAAAGSTTTCTAGAGACAAACAGCCGGCTCTAATTA
TTTTTTCGAACCTTACGCTTGAGTAAAGATCTGCAAATGGCAACCCTACCTATACTATTAA
AATATAATGTTACATTCTGATCTGAATGTTTAAATAATCACTTCATATTCTGTTGCGAG

Domäne e

ATTCTGCCCCACACAGATGATGGACACACTGAACCAGTGATGATTGCAAGATATCACACA
ATTGGACAAGCGTCAACAACCTGTCAGTGGTGAAGCCCTCGAGTCCATGAAAGCCGACCA
TCATCTGATGGGTTCCAGGCAATCGCTTCCTTCCATGCTCTTCCCTCCTTTGTCCATCAC
CAGCTGCTTCAAAGAGGTTTGGCTGCTGCGTCCATGGCATGCCAACCTTCCCGCAATG

Figur 9

Abgeleitete Primärstruktur des KLH1

Domäne b

GLPYWDWTEPMTHIPGLAGNKTYVDSHGASHTNPFHSSVIAFEENAPHTKRQIDQRLFKPA
TFGHHTDLFNQILYAFEQEDYCDFEVQFEITHNTIHAWTGGSEHFSMSSLHYTAFDPLFYF
HHSNVDRWLWAVWQALQMRRHKPYRAHCAISLEHMLKPFAPSSPLNNNEKTHANAMPNKIV
DYENVLHYTYEDLTFGGISLENIEKMIHENQQEDRIYAGFLLAGIRTSANVDIFIKTDSV
QHKAGTFAVLGGSKEMKWGFDRVFKFDITHVLKDLDLTADGDFEVTVDITEVDGTKLASSL
IPHASVIREHARGKLNK

Domäne c

VKFDKVPRSRIRKKNVDRLSPEEMNELRKALALLKEDKSAGGFQQLGAFHGEPKWCPSPEA
SKKFACCVHGMSVFPWHRLLTVOSENALRRHGYDGAALPYWDWTSPLNHLPELADHEKYVD
PEDGVEKHNPWFDDGHIDTVDKTTTRSVQNKLFEOPEFGHYTSIAKQVLLALEQDNFCDFEI
QYEIAHNYTHALVGGAQPYGMASLRYTAFDPLFYLLHHSNTDRIWAIWQALQKYRGKPYNVA
NCAVTSMREPLQPFGLSANINTDEVTKEHSVPFNVFDYKTNFNYEYDTLEFNGLSISOLNK
KLEAIKSQDRFFAGFLLSGFKKSSLVKFNICTDSSNCHPAGEFYLLGDENEMPWAYDRVFK
YDITEKLHDLKLHAEDHFIYIDYEVFDLKPASLGKDLFKQPSVIHEPRI

Domäne d

GHHEGEVYQAEVTSANRIRKNIENLSLGELESLRAAFLEIENDGTYESIAKFHGSPGLCQL
NGNPISCCVHGMPFPHWRRLYVVVVENALLKKGSSVAVPYWDWTKRIEHLPHLISDATYY
NSRQHMYETNPFHHGKIETHENEITTRDPKDSLPHSDYFYEQVLYALEQDNFCDFEIQLEIL
HNAHSLGKGKYSMSNLDYAAFDPVFFLHATTDRIWAIWQDLQRFKRKPYREANCAIQ
LMHTPLQPFDKSDNNDEATKTHATPHDGFYQNSFGYAYDNLELNHYSIPOLDHMLQERKR
HDRVFAFGLLNIGTSADGHVFCVCLPTGEHTKDCSHEAGMFSILGGQTEMSFVFDRLYKLD
ITKALKKNGVHLQGDFFLEIEITAVNGSHLDSHVIHSPTILFEAG

Domäne e

DSAHTDDGHTEPVMIRKDITQLDKRQQLSLVKALESMKADHSSDGFQAIASFHALPPLCPS
PAASKRFACCVHGMPFPHWRRLYTVQFQDSLKKGAVVGLPYWDWTLPR

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Figur 10

cDNA-Sequenz in Verbindung mit Intronstruktur des KLH2

Domäne b

GGCCTGCCCTACTGGGATTGGACCATGCCAATGAGTCATTTGCCAGAACTGGCTACAAGTG
 AGACCTACCTCGATCCAGTTACTGGGGAAACTAATAACAACCCTTTCCATCACGCCCAAGT
 GGCGTTTGAATAATGGTGTAAACAAGCAGGAATCCTGATGCCAAACTTTTTATGAAACCACT
 TACGGAGACCACACTTACCTCTTCGACAGCATGATCTACGCATTTGAGCAGGAAGACTTCT
 GCGACTTTGAAGTCCAATATGAGCTCACGCATAATGCAATACATGCATGGGTTGGAGGCAG
 TGAATAAGTATTCAATGTCTTCTCTTCACTacacTGCTTTTGATCCTATATTTTACCTCCAT
 CACTCAAATGTTGATCGTCTCTGGGCCATTTGGCAAGCTCTTCAAATCAGGAGAGGCAAGT
 CTTACAAGGCCCACTGCGCCTCGTCTCAAGAAAGAGAACCATTAAAGCCTTTTGCATTTCAG
 TTCCCCACTGAACAACAACGAGAAAACGTACCACAACCTCTGTCCCCACTAACGTTTATGAC
 TATGTGGGAGTTTTGCACATATCGATATGATGACCTTCAGTTTGGCGGTATGACCATGTTCAG
 AACTTGAGGAATATATTTACAAGCAGACACAACATGATAGAACCCTTTGCAGGATTCTTCCT
 TTCATATATTGGAACATCAGCAAGCGTAGATATCTTCATCAATCGAGAAGGTCATGATAAA
 TACAAAGTGGGAAGTTTTGTAGTACTTGGTGGATCCAAAGAAATGAAATGGGGCTTTGATA
 GAATGTACAAGTATGAGATCACTGAGGCTCTGAAGACGCTGAATGTTGCASTGGATGATGG
 GTTCAGCATTACTGTTGAGATCACCGATGTTGATGGATCTCCCCCATCTGCAGATCTCATT
 CCACCTCCTGCTATAATCTTTGaACGTGGTCaTG

Intron 2b/c

AGGTATTTAAAAAAGTAATAAAAACCaTATTTTCGAATGCGCTTTATGAAATATCGTGTGAC
 TGGTTCTTTAGTTTACATGGAGTGTAAACAACATGCTCCATCAGTTGACATATACTGCTCAC
 ACAAGTAAGGGATATTTGATAATGATAACAAATATAATCAAAGCGGTTATACTATCAAGA
 CTTATTACATAATTACAGGTGAAGGGAGGTGTGATCGTGTTCAGTATCAGGTTGAGGCC
 AGAGAAGTCCCAAGTTTGAAGTCTTGACAGAAGATGATGTTTAGGCATGGGGTCGAATCACCAA
 AATCACATGACTTCAATAACGGGTTGGACCACCTCGAGCGACgATGCAAGCAGTAGAGCGT
 CTACGCATGCTCCTGATAAGGCGACCAATCTGTTTCTGGGGAATCAGtCGCCACTCCTCTT
 GTAGTGCCACGCTCATTTCTGCTACGGTCTGGGTACCTGCTATCGGgTCTTGATCCGTAT
 CCCAAGGATGTCCACACATGTTCAAgGTGAGAGGTGGGGAAACATCGCTGGCCACGGTaA
 GGtCTGAATTTGATGCCGTTGAAAGTGAAGCTCTGACAACcTGAGCATGGtGAGCTCTGACG
 TTGTCGTCCTGAAAGATGAATcCAGCTcCaTGaCAGCGAGCAAaGGGCAGGACGTGTTGGT
 CAATGCAGTTGTCTCTGCAGTACACACCTGTCACTCGCCACTCACAAAGCGTGTAGATCTGT
 ACGACCAGTCATGGAGATCCCAGCCCACATCATAACGGACCCCTATCCATACCGATCATGA
 GCCACCATAGCAGCGTCTTGATGACGTTCTCCCTGTGCGCTCGACATCCTcACACGGCCAA
 AAGGAACGTGGACTCGTCACTGAACATGACATTAGCCAACCTGGCACTTGTCCACCGCTGA
 TGTTGGCGAGACCATTCCAGTCGAGCTCTTCGGTGTCTGGCTTTTCATCGATAACACGACGT
 AAGGTCTGCGGGGCTGCAAGACGGCTCTATGCAAGGCGATTTTCGGATTGTCTGGGTGCTAAC
 TCTGATCCCAGGTGCCTGCTGAAGTTGATGCTGGATCTGTGTGGCATTGAGATGGCGATTC
 CTTAGGACTGTGGAGATGATGAATCGATCTTGACTTATGGTGGTGACATTAGGACGTGGGG
 TTCGTGTCTTATCCTGCACTCTTCCAGTTGTTTCGGTGACGCTCTGGTACCGGCTGATTAC
 TGACTGAGAATATCCATCTGCCGTGCGACATGAGCCTGTGTTGGCCCAGCCTGAAGCATTG
 CAATCGCCAGAGACGCTCTTCAAAGTCAATTCGACGCATGGtTTTCTGTTCAAAATGACA
 GCGTAAACAGtTTTTGGtGCTTTTATGCTTCCCAAGAGCATGAAAAACACGTTCTATgGG
 TCGtGCACACCTTACATGACAAGtGtGAAAAGTGACTTGcACCCCTTGTgGtGTTCCGATG
 CACACTCTGTTTACGTACTGATGCGATTTGGCGTCTAAACATGTTTTGGCGTCTAAACATG
 FTTTCTGTCATGATTCATATACTATTTTTGTATATTCTGGCATCAAACCAACTACAGTG
 AAATATATTTCAATATCCCCTACTTTGTGTGAGTAGTATAGATCACTGCAGACAACATATA

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GACAAAGCAgTtTaCaCCGTCAAACAATCCAGTCATTAATTATGATGaCaCTTCCACACATA
GFGTCAGTGATTGTAATTCAaCTGTACACACTTTTCCCGTGAACATTTCAGGATCTATATGA
CTAAATATATAACATTAGTATACGTGCAGTTTTGTATCGCTACGACATTGTTGTAACCTCTT
TGTTTTAATCATTTaACAG

Domäne c

CTGATGCCAAGaCTTTGgCCATAGCAGAAAAATCAGgAAAGcCGTTGATTcTcTGACAGT
CgAAGAACAaaCTTCGTTGAGgCGAGcTATGgCAGATcTACAGGACGACAAAACATCAGGG
GGTTTTCCAGCAGATTGCAGCATTCACCGGAGAACCAAAATGTTGTCCAAGCCCCgAAGCGG
AGAAAAAATTTGCATGCTGTGTTCATGGAAATGGCTGTTTTCCCTCACTGGCACAGATTGCT
GACAGTTCAAGGAGAAATGCTCTGAGGAACACTGGCTTTACTGGTGGACTGCCCTACTGG
GACTGGACTCGATCAATGAGCGCCCTTCCACATTTTGTGTGCTGATCCTACTTACAATGATG
CTATTTCCAGCCAGGAAGAAGATAACCCATGGCATCATGGTCACATAGACTCTGTTGGGCA
TGATACTACAAGAGATGTGCGTGATGATCTTTATCAATCTCCTGGTTTTCGGTCACTACACA
GATATTGCACAACAAGTCCTTCTGGCCTTTGAGCAGGACAGTTTCTGTGATTTTGAGGTAC
AATTTGAAATTGCCCATAAATTCATACATGCACTGATTGGTGGTAACGAACCATACAGTAT
GTCATCTTTGAGGTATACTACATACATCAATCTTCTTCTTGCACTCAGTACAGAC
CGACTTTGGGCGCATCTGGCAAGCAATCACTAGTGCGGCCCGCTGCAGGTCGACCATAAGGG
AGAGCTCCCAACGCgtTGGAtGCAATCT

Domäne c

ATGGCTGTGTTTCCGCACTGGCACAGACTGTTTGTGAAACAGATGGAGGACGCACTTGCTG
CTCATGGAGCTCATATTGGCATACCATACTGGGATTGGACAAGTGCCTTTAGTCATCTGCC
CGCCCTAGTGACTGACCACGAGAACAAATCCCTTCCACCAC

Intron c(2)

GTATGTGTCAAATCGITTTTAGGAACTGCCTTATCCATTTTACAATTACGAGTACAAAATGA
AAACGGAAACTGTGTGACCTCGAAAAGTGCAATCTTTAAAGGATGCAATGTACACAATLAA
ATGCTCCGATCAAAGCGATGGCTGAGAATCATTTTCCCTCTAATTCCCTTTACACACAGCT
CGGTTCTGTTTTAAGTAGGAACAAGTCTCTGCAAAAACATCACAAATLALAGAGACACAGAA
AAAACCTCATTTCTCGTTTTCTGTATTCCGAAAATGAATTTTACAATTTCTTTTATAG

Domäne c

GGCCATATTGGTCATCTGAATGTGGATACATCTCGATCTCCAAGAGACATGCTGTTTAATG
ATCCTGAACAAGGCTCAGAATCATTCTTCTACAGACAGGTTCTCTTGACTCTAGAACAGAC
AGACTTCTGCCAATTGTGAAGTTTCAGTTTGAACCTTACACACAATGCCATCCACTCTTGGACT
GGAGGACATACTCCPATATGGAATGTCATCACTGGAATATACAGCATATGATCCACTCTTTT
ATCTCCACCATTCCAACACTGATCGTATCTGGGCCATCTGGCAGGCACCTCCAGAAATATAG
AGGTCTTCCATACAAGCAGCTCACTGCGATATccaaagttctgaaacaaaccttTAAACCA
TTCAGCGAGTCCAGGAATCCAAACCCAGTCCACAGGCCAATTCTATAGGGCCGTTGATTTCAT
TTGATTATGAGAAATTCAATTATCAATATGACACACTTACCTTCCACGGACTTCTATCCC
AGAACTTGATGCCATGCTTCAAGAGAGAAAGAAGGAAGAGAGAACATTTGCAGCCTTCCTG
TTGCACGGATTTGGCGCCAGTGCTGATGTTTCGTTTGATGTCTGCACACCTGATGGTCATT
GTGCCCTTTGCTGGAACCTTCGCGGTACTTGGTGGGGAGCTTGAGATGCCCTGGTCCTTTGA
AAGATTGTTCCGTTACGATATCACAAAGGTTCTCAAGCAGATGAATCTTCACTATGATTCT
GAGTCCCACTTTGAGTTGAAGATTGTTGGCACAGATGGTACAGAACTGCCATCGGATCGTA
TCAGAGGCCCTACCATTGAACACCATTGGAGGAG

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Intron g/h

GTATGTTTTGAGATCCACATAATCTTCTACCCTGTCTCATTTCTAATGCTCTTCAATACAC
AATTTATATAGCCTTTGAGCTTCAGATGTATTACGGACAGGCATTACAGTATACATGTAAT
ATGGTTTTTCTGCTATTTGCAAAAATTGTGTCCTATCTCTGTTTCAGATCATCATGGCGGTGA
CACCTAG

Domäne h

GTCACGATCACAGTGAACGTCACGATGGATTTTTTCAGGAAGGAAGTCGGTTCCTGTCCCT
GGATGAAGCCAATGACCTTAAAAATGCACTGTACAAGCTGCAGAATGATCAGGGTCCCAAT
GGATATGAATCAATAGCCGGTTACCATGGCTATCCATTCCTCTGCCCTGAACATGGTGAAG
ACCAGTACGCATGCTGTGTCCACGGAATGCCTGTATTTCCACATTGGCACAGACTTCATAC
AATCCAGTTTGAGAGAGCTCTCAAAGAACATGGTTCTCATTTGGGTCTGCCATACTGGGAC
TGGAC

Figur 11

Abgeleitete Primärstruktur von KLH2

Domäne b

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DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare:

That my residence, post office address and citizenship are as stated below next to my name.

That I verily believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **NUCLEIC ACID MOLECULE COMPRISING A NUCLEIC ACID SEQUENCE CODING FOR A HAEMOCYANIN** the specification of which (check one)

☒ is attached hereto.

☐ was filed on _____ as Application, Serial No. _____ and was amended on _____ (if applicable).

That I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

That I acknowledge the duty to disclose information known to be material to patentability of this application in accordance with Title 37, Code of Federal Regulations §1.56(a).

That I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate on this invention having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)**Priority Claimed**

PCT/EP00/02410 Europe 17 March 2000
(Number) (Country) (Day/Month/Year Filed)

☒ ☐
Yes No

199 11 971.6 Germany 17 March 1999
(Number) (Country) (Day/Month/Year Filed)

☒ ☐
Yes No

199 39 578.0 Germany 20 August 1999
(Number) (Country) (Day/Month/Year Filed)

☒ ☐
Yes No

That I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

United States Application(s)

(Application Serial No.) (Filing Date) (Status)-(Patented, pending, abandoned)

(Application Serial No.) (Filing Date) (Status)-(Patented, pending, abandoned)

(Application Serial No.) (Filing Date) (Status)-(Patented, pending, abandoned)

That all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

I hereby appoint the following attorneys, with full power of substitution and revocation, to prosecute this application and to transact all business in the United States Patent and Trademark Office connected therewith and request that all correspondence and telephone calls in respect to this application be directed to: WELSH & KATZ, LTD., 120 South Riverside Plaza, 22nd Floor, Chicago, Illinois 60606-3913, Telephone No.: (312) 655-1500:

AttorneyRegistration No.

A. Sidney Katz
 Richard L. Wood
 Jerold B. Schnayer
 Eric C. Cohen
 Joseph R. Marcus
 Gerald S. Schur
 Gerald T. Shekleton
 James A. Scheer
 Daniel R. Cherry
 Kathleen A. Rheintgen
 Edward P. Gamson
 Thomas W. Tolpin
 Shannon L. Nebolsky
 Mitchell J. Weinstein
 Charles R. Krikorian

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Full name of sole or one joint inventor:

Inventor's signature:

Date:

Residence and Post Office Address:

Jürgen MARKL

M. Markl
 2. Oct. 01

An der Mahlsteig 12

55296 Gau-Bischofsheim

GERMANY

Germany

Citizenship:

Full name of additional joint inventor, if any:

Inventor's signature:

Date:

Residence and Post Office Address:

Benjamin ALTENHEIN

B. Altenhein
 4. 10. 01

Elasser Platz 7 ELSAESSER PLATZ 7

65195 Weisbaden

GERMANY

Germany

Citizenship:

SEQUENCE LISTING

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5

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<210> 9

<211> 1003

<212> DNA

<213> Haliotis tuberculata

<400> 9

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<210> 10

<211> 1251

<212> DNA

<213> Haliotis tuberculata

<400> 10

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6

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<210> 11

<211> 1244

<212> DNA

<213> *Haliotis tuberculata*

<400> 11

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<210> 12

<211> 1255

<212> DNA

<213> *Haliotis tuberculata*

<400> 12

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7

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<210> 13

<211> 1248

<212> DNA

<213> *Haliotis tuberculata*

<400> 13

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<210> 14

<211> 1207

<212> DNA

<213> *Haliotis tuberculata*

<400> 14

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8

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<210> 15

<211> 1546

<212> DNA

<213> *Haliotis tuberculata*

<400> 15

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<210> 16

<211> 967

<212> DNA

<213> *Megathura crenulata*

<400> 16

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9

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<210> 17

<211> 1242

<212> DNA

<213> Megathura crenulata

<400> 17

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<213> *Haliotis tuberculata*

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16

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<213> Haliotis tuberculata

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4

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<211> 1209

<212> DNA

<213> *Haliotis tuberculata*

<400> 7

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<210> 8

<211> 1535

<212> DNA

<213> *Haliotis tuberculata*

<400> 8

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5

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<210> 9
 <211> 1003
 <212> DNA
 <213> Haliotis tuberculata

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 <213> Haliotis tuberculata

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6

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<210> 11

<211> 1244

<212> DNA

<213> *Haliotis tuberculata*

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<210> 12

<211> 1255

<212> DNA

<213> *Haliotis tuberculata*

<400> 12

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7

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<210> 13

<211> 1248

<212> DNA

<213> *Haliotis tuberculata*

<400> 13

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<210> 14

<211> 1207

<212> DNA

<213> *Haliotis tuberculata*

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9

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<211> 1242

<212> DNA

<213> Megathura crenulata

<400> 17

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gtggatttca	gcagcttggg	gcattccatg	gggagccaaa	atggtgtcct	agtcccgaag	180
catctaaaaa	atttgccctgc	tgtgttcacg	gcatgtctgt	gttcctcac	tggcatcgac	240
tgttgacggg	tcagagtga	aatgctttga	gacgacatgg	ctacgatgga	gctttgccgt	300
actgggattg	gacctctcct	cttaatcacc	ttcccgaact	ggcagatcat	gagaagtacg	360
tcgaccctga	agatggggta	gagaagcata	acccttgggt	cgatgggtcat	atagatacac	420
tcgacaaaac	aacaacaaga	agtgttcaga	ataaactcct	cgaacagcct	gagtttggtc	480
attatacaag	cattgccaaa	caagtactgc	tagcgttggg	acaggacaat	ttctgtgact	540
ttgaaatcca	atatgagatt	gcccataact	acatccatgc	acttgttagg	ggcgctcagc	600
cttatgggat	ggcatcgctt	cgctacactg	cttttgatcc	actattctac	ttgcatcact	660
ctaatacaga	tcgtatatgg	gcaatatggc	aggctttaca	gaagtacaga	ggaaaaccgt	720
acaacgttgc	taactgtgct	gttacatcga	tgagagaacc	tttgcaacca	tttggcctct	780
ctgccaatat	caacacagac	catgtaacca	aggagcattc	agtgccattc	aacgtttttg	840
attacaagac	caatttcaat	tatgaatatg	acactttgga	atttaacggg	ctctcaatct	900
ctcagttgaa	taaaaagctc	gaagcgataa	agagccaaga	caggttcctt	gcaggcttcc	960
tgttatctgg	tttcaagaaa	tcctctcttg	ttaaattcaa	tatttgacc	gatagcagca	1020
actgtcaccc	cgctgggag	ttttaccttc	tgggtgatga	aaacgagatg	ccatgggcat	1080
acgatagagt	cttcaaatat	gacataaccg	aaaaactcca	cgatctaaag	ctgcatgcag	1140
aagaccactt	ctacattgac	tatgaagtat	ttgaccttaa	accagcaagc	ctgggaaaag	1200
atttgttcaa	gcagccttca	gtcattcatg	aaccaagaat	ag		1242

<210> 18

<211> 1236

<212> DNA

<213> Megathura crenulata

<400> 18

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acattgaaaa	tctgagcctt	ggtgaactcg	aaagtctgag	agctgccttc	ctggaaattg	120
aaaacgatgg	aacttacgaa	tcaatagcta	aattccatgg	tagccctggg	ttgtgccagt	180
taaatggtaa	ccccatctct	tgttggtgct	atggcatgcc	aactttccct	cactggcaca	240
gactgtacgt	ggttgtcggt	gagaatgccc	tcctgaaaaa	aggatcatct	gtagctgttc	300
cctattggga	ctggacaaaa	cgaatcgaac	atttacctca	cctgatttca	gacgccactt	360
actacaattc	caggcaacat	cactatgaga	caaaccatt	ccatcatggc	aaaatcacac	420
acgagaatga	aatcactact	agggatccca	aggacagcct	cttccattca	gactactttt	480
acgagcaggt	cctttacgcc	ttggagcagg	ataacttctg	tgatttcgag	attcagttgg	540
agatattaca	caatgcattg	cattctttac	ttgggtggca	aggtaaatat	tccatgtcaa	600
accttgatta	cgctgctttt	gatcctgtgt	tcttccctca	tcacgcaacg	actgacagaa	660
tctgggcaat	ctggcaagac	cttcagaggt	tccgaaaacg	gccataccga	gaagcgaatt	720

10

gcgctatcca attgatgcac acgccactcc agccgtttga taagagcgac aacaatgacg 780
aggcaacgaa aacgcatgcc actccacatg atgggtttga atatcaaaac agctttgggtt 840
atgcttacga taatctggaa ctgaatcact actcgattcc tcagcttgat cacatgctgc 900
aagaaagaaa aaggcatgac agagtattcg ctggcttcct cttcacaat attggaacat 960
ctgöcgcgatgg ccattgtattt gtatgtctcc caactgggga acacacgaag gactgcagtc 1020
atgaggctgg tatgtttctcc atcttaggcg gtcaaacgga gatgtccttt gtatttgaca 1080
gactttacaa acttgacata actaaagcct tgaaaaagaa cgggtgtgcac ctgcaagggg 1140
atttcgatct ggaaattgag attacggctg tgaatggatc tcacttagac agtcattgtca 1200
tccactctcc cactatactg tttgaggccg gaacag 1236

<210> 19
<211> 241
<212> DNA
<213> Megathura crenulata

<400> 19
attctgcccc cacagatgat ggacacactg aaccagtgat gattcgcaaa gatatacacac 60
aattggacaa gcgtcaacaa ctgtcactgg tgaaagccct cgagtccatg aaagccgacc 120
attcatctga tgggttccag gcaatcgctt ccttccatgc tcttctcctt ctttgtccat 180
caccagctgc ttcaaagagg tttgcgtgct gcgtccatgg catgccaacc ttcccgcaat 240
g 241

<210> 20
<211> 949
<212> DNA
<213> Megathura crenulata

<400> 20
ggcctgccct actgggattg gaccatgcca atgagtcatt tgccagaact ggctacaagt 60
gagacctacc tcgatccagt tactggggaa actaaaaaca accctttcca tcacgccccaa 120
gtggcgtttg aaaatgggtgt aacaagcagg aatcctgatg ccaaactttt tatgaaacca 180
acttacggag accacactta cctcttcgac agcatgatct acgcatttga gcaggaagac 240
ttctgcgact ttgaagtcca atatgagctc acgcataatg caatacatgc atggggttga 300
ggcagtga aaagtattcaat gtcttctctt cactacactg cttttgatcc tatattttac 360
ctccatcact caaatgttga tcgtctctgg gccatttggc aagctcttca aatcaggaga 420
ggcaagtctt acaaggccca ctgcgcctcg tctcaagaaa gagaaccatt aaagcctttt 480
gcattcagtt cccactgaa caacaacgag aaaacgtacc acaactctgt cccactaac 540
gtttatgact atgtgggagt tttgcactat cgatatgatg accttcagtt tggcgggatg 600
accatgtcag aacttgagga atatattcac aagcagacac aacatgatag aacctttgca 660
ggattcttcc ttccatata tggaaacatca gcaagcgtag atatcttcat caatcgagaa 720
ggtcatgata aatacaaaagt ggggaagtttt gtagtacttg gtggatccaa agaaatgaaa 780
tggggctttg atagaatgta caagtatgag atcactgagg ctctgaagac gctgaatgtt 840
gcagtggatg atgggttcag cattactgtt gagatcccg atgttgatgg atctccccca 900
tctgcagatc tcattccacc tctgtctata atctttgaac gtgggtcatg 949

<210> 21
<211> 760
<212> DNA
<213> Megathura crenulata

<400> 21
ctgatgccaa agactttggc catagcagaa aaatcaggaa agccgttgat tctctgacag 60
tcgaagaaca aacttcgttg aggcgagcta tggcagatct acaggacgac aaaacatcag 120
ggggtttcca gcagattgca gcattccacg gagaacccaa atgggtgtcca agccccgaag 180
cggagaaaaa atttgcattg tgtgttcatt gaattggtgt tttccctcac tggcacagat 240
tgctgacagt tcaaggagaa aatgctctga ggaaacatgg ctttactggg ggactgcctt 300

11

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actgggactg gactcgatca atgagcgccc ttccacattt tgttgetgat cctacttaca 360
atgatgctat ttccagccag gaagaagata acccatggca tcatgggtcac atagactctg 420
ttgggcatga tactacaaga gatgtgcgtg atgatcttta tcaatctcct ggtttcggtc 480
actacacaga tattgcacaa caagtccttc tggcctttga gcaggacagt ttctgtgatt 540
ttgaggtaca atttgaaatt gcccataatt tcatacatgc actgattggg ggtaacgaac 600
catacagtat gtcacatctt aggtatacta catacagatc aatcttcttc ttgcaccact 660
ccagtacaga ccgacttttg gccatctggc aagcaatcac tagtgcgggc gcctgcaggt 720
cgaccataag ggagagctcc caacgcgttg gatgcaatct 760
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<210> 22
 <211> 323
 <212> DNA
 <213> Megathura crenulata

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<400> 22
gttcacacca ggctgatgaa tategtgagg cagtaacaag cgctagccac ataagaaaaa 60
atatccggga cctctcagag ggagaaattg agagcatcag atctgctttc ctccaaattc 120
aaaaagaggg tatatatgaa aacattgcaa agttccatgg aaaaccagga ctttgtgaac 180
atgatggaca tcctgttgct tgttgtgtcc atggcatgcc cacctttccc cactggcaca 240
gactgtacgt tcttcagggt gagaatgcgc tcttagaacg agggctctgca gttgctgttc 300
cttactggga ctggacccta cct 323
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<210> 23
 <211> 988
 <212> DNA
 <213> Megathura crenulata

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<400> 23
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gctcatggag ctcatatttg cataccatac tgggattgga caagtgcgtt tagtcatctg 120
cccgccctag tgactgacca cgagaacaat cccttcacc acggccatat tgggtcatctg 180
aatgtggata catctcgatc tccaagagac atgctgttta atgatcctga acaaggctca 240
gaatcattct tctacagaca ggttctcttg actctagaac agacagactt ctgccaattt 300
gaagttcagt ttgaacttac acacaatgcc atccactctt ggactggagg acatactcca 360
tatggaatgt catcactgga atatacagca tatgatccac tcttttatct ccaccattcc 420
aacactgacg gtatctgggc catctggcag gcaactccaga aatatagagg tcttccatac 480
aacgcagctc actgcgatat ccaagttctg aaacaacctc ttaaaccatt cagecgagtcc 540
aggaatccaa acccagtcac cagagccaat tctagggccg ttgattcatt tgattatgag 600
aaattcaatt atcaatatga cacacttacc ttccacggac tttctatccc agaacttgat 660
gccatgcttc aagagagaaa gaaggaagag agaacatttg cagccttcct gttgcacgga 720
tttggcgcca gtgctgatgt ttcgtttgat gtctgcacac ctgatggcca ttgtgccttt 780
gctggaacct tcgcgttact tgggtggggag cttgagatgc cctgggtcctt tgaaagattg 840
ttcgtttacg atatcacaaa ggttctcaag cagatgaatc ttcactatga ttctgagttc 900
cactttgagt tgaagattgt tggcacagat ggaacagaac tgccatcgga tcgtatcaag 960
agccctacca ttgaacacca tggaggag 988
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<210> 24
 <211> 310
 <212> DNA
 <213> Megathura crenulata

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<400> 24
gtcacgatca cagtgaacgt cacgatggat ttttcaggaa ggaagtcggt tccctgtccc 60
tggaatgaag caatgacctt aaaaatgcac tgtacaagct gcagaatgat caggggtccc 120
atggatatga atcaatagcc gggtaccatg gctatccatt cctctgccct gaacatgggt 180
aagaccagta cgcattgctg gtccacggaa tgccgtgatt tccacattgg cacagacttc 240
atacaatcca gtttgagaga gctctcaaa aacatggttc tcaattgggt ctgccatact 300
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gggactggac

310

<210> 25

<211> 422

<212> PRT

<213> *Haliotis tuberculata*

<220>

<221> SIGNAL

<222> (1) . . (15)

<400> 25

Leu Val Gln Phe Leu Leu Val Ala Leu Val Ala Gly Ala Gly Ala Asp
1 5 10 15

Asn Val Val Arg Lys Asp Val Ser His Leu Thr Asp Asp Glu Val Gln
20 25 30

Ala Leu His Gly Ala Leu His Asp Val Thr Ala Ser Thr Gly Pro Leu
35 40 45

Ser Phe Glu Asp Ile Thr Ser Tyr His Ala Ala Pro Ala Ser Cys Asp
50 55 60

Tyr Lys Gly Arg Lys Ile Ala Cys Cys Val His Gly Met Pro Ser Phe
65 70 75 80

Pro Phe Trp His Arg Ala Tyr Val Val Gln Ala Glu Arg Ala Leu Leu
85 90 95

Ser Lys Arg Lys Thr Val Gly Met Pro Tyr Trp Asp Trp Thr Gln Thr
100 105 110

Leu Thr His Leu Pro Ser Leu Val Thr Glu Pro Ile Tyr Ile Asp Ser
115 120 125

Lys Gly Gly Lys Ala Gln Thr Asn Tyr Trp Tyr Arg Gly Glu Ile Ala
130 135 140

Phe Ile Asn Lys Lys Thr Ala Arg Ala Val Asp Asp Arg Leu Phe Glu
145 150 155 160

Lys Val Glu Pro Gly His Tyr Thr His Leu Met Glu Thr Val Leu Asp
165 170 175

Ala Leu Glu Gln Asp Glu Phe Cys Lys Phe Glu Ile Gln Phe Glu Leu
180 185 190

Ala His Asn Ala Ile His Tyr Leu Val Gly Gly Lys Phe Glu Tyr Ser
195 200 205

Met Ser Asn Leu Glu Tyr Thr Ser Tyr Asp Pro Ile Phe Phe Leu His
210 215 220

His Ser Asn Val Asp Arg Leu Phe Ala Ile Trp Gln Arg Leu Gln Glu
225 230 235 240

13

Pro	His	Trp	His	Arg	Leu	Phe	Val	Thr	Gln	Val	Glu	Asp	Ala	Leu	Val	85	90	95
Arg	Arg	Gly	Ser	Pro	Ile	Gly	Val	Pro	Tyr	Trp	Asp	Trp	Thr	Lys	Pro	100	105	110
Met	Thr	His	Leu	Pro	Asp	Leu	Ala	Ser	Asn	Glu	Thr	Tyr	Val	Asp	Pro	115	120	125
Tyr	Gly	His	Thr	His	His	Asn	Pro	Phe	Phe	Asn	Ala	Asn	Ile	Ser	Phe	130	135	140
Glu	Glu	Gly	His	His	His	Thr	Ser	Arg	Met	Ile	Asp	Ser	Lys	Leu	Phe	145	150	155
Ala	Pro	Val	Ala	Phe	Gly	Glu	His	Ser	His	Leu	Phe	Asp	Gly	Ile	Leu	165	170	175
Tyr	Ala	Phe	Glu	Gln	Glu	Asp	Phe	Cys	Asp	Phe	Glu	Ile	Gln	Phe	Glu	180	185	190
Leu	Val	His	Asn	Ser	Ile	His	Ala	Trp	Ile	Gly	Gly	Ser	Glu	Asp	Tyr	195	200	205
Ser	Met	Ala	Thr	Leu	His	Tyr	Thr	Ala	Phe	Asp	Pro	Ile	Phe	Tyr	Leu	210	215	220
His	His	Ser	Asn	Val	Asp	Arg	Leu	Trp	Ala	Ile	Trp	Gln	Ala	Leu	Gln	225	230	235
Ile	Arg	Arg	His	Lys	Pro	Tyr	Gln	Ala	His	Cys	Ala	Gln	Ser	Val	Glu	245	250	255
Gln	Leu	Pro	Met	Lys	Pro	Phe	Ala	Phe	Pro	Ser	Pro	Leu	Asn	Asn	Asn	260	265	270
Glu	Lys	Thr	His	Ser	His	Ser	Val	Pro	Thr	Asp	Ile	Tyr	Asp	Tyr	Glu	275	280	285
Glu	Val	Leu	His	Tyr	Ser	Tyr	Asp	Asp	Leu	Thr	Phe	Gly	Gly	Met	Asn	290	295	300
Leu	Glu	Glu	Ile	Glu	Glu	Ala	Ile	His	Leu	Arg	Gln	Gln	His	Glu	Arg	305	310	315
Val	Phe	Ala	Gly	Phe	Leu	Leu	Ala	Gly	Ile	Gly	Thr	Ser	Ala	Leu	Val	325	330	335
Asp	Ile	Phe	Ile	Asn	Lys	Pro	Gly	Asn	Gln	Pro	Leu	Lys	Ala	Gly	Asp	340	345	350
Ile	Ala	Ile	Leu	Gly	Gly	Ala	Lys	Glu	Met	Pro	Trp	Ala	Phe	Asp	Arg	355	360	365
Leu	Tyr	Lys	Val	Glu	Ile	Thr	Asp	Ser	Leu	Lys	Thr	Leu	Ser	Leu	Asp	370	375	380

His Ala Leu Val Gly Gly Thr Asp Ala Tyr Gly Met Ala Ser Leu Arg
195 200 205

Tyr	Thr	Ala	Tyr	Asp	Pro	Ile	Phe	Phe	Leu	His	His	Ser	Asn	Thr	Asp
	210					215					220				
Arg	Ile	Trp	Ala	Ile	Trp	Gln	Ser	Leu	Gln	Lys	Tyr	Arg	Gly	Lys	Pro
225					230					235					240
Tyr	Asn	Thr	Ala	Asn	Cys	Ala	Ile	Glu	Ser	Met	Arg	Arg	Pro	Leu	Gln
				245					250					255	
Pro	Phe	Gly	Leu	Ser	Ser	Ala	Ile	Asn	Pro	Asp	Arg	Ile	Thr	Arg	Glu
			260					265					270		
His	Ala	Ile	Pro	Phe	Asp	Val	Phe	Asn	Tyr	Arg	Asp	Asn	Leu	His	Tyr
		275					280					285			
Val	Tyr	Asp	Thr	Leu	Glu	Phe	Asn	Gly	Leu	Ser	Ile	Ser	Gln	Leu	Asp
	290					295					300				
Arg	Glu	Leu	Glu	Lys	Ile	Lys	Ser	His	Glu	Arg	Val	Phe	Ala	Gly	Phe
305					310					315					320
Leu	Leu	Ser	Gly	Ile	Lys	Lys	Ser	Ala	Leu	Val	Lys	Phe	Glu	Val	Cys
				325					330					335	
Thr	Pro	Pro	Asp	Asn	Cys	His	Lys	Ala	Gly	Glu	Phe	Tyr	Leu	Leu	Gly
			340					345					350		
Asp	Glu	Asn	Glu	Met	Ala	Trp	Ala	Tyr	Asp	Arg	Leu	Phe	Lys	Tyr	Asp
		355					360					365			
Ile	Thr	Gln	Val	Leu	Glu	Ala	Asn	His	Leu	His	Phe	Tyr	Asp	His	Leu
	370					375					380				
Phe	Ile	Arg	Tyr	Glu	Val	Phe	Asp	Leu	Lys	Gly	Val	Ser	Leu	Gly	Thr
385					390					395					400
Asp	Leu	Phe	His	Thr	Ala	Asn	Val	Val	His	Asp	Ser	Gly	Thr		
				405					410						

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<210> 28
<211> 413
<212> PRT
<213> Haliotis tuberculata
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<400> 28
Gly Thr Arg Asp Arg Asp Asn Tyr Val Glu Glu Val Thr Gly Ala Ser
 1           5           10           15
His Ile Arg Lys Asn Leu Asn Asp Leu Asn Thr Gly Glu Met Glu Ser
          20           25           30
Leu Arg Ala Ala Phe Leu His Ile Gln Asp Asp Gly Thr Tyr Glu Ser
          35           40           45
Ile Ala Gln Tyr His Gly Lys Pro Gly Lys Cys Gln Leu Asn Asp His
 50           55           60

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17

Asn Ile Ala Cys Cys Val His Gly Met Pro Thr Phe Pro Gln Trp His
65 70 75 80

Arg Leu Tyr Val Val Gln Val Glu Asn Ala Leu Leu Asn Arg Gly Ser
85 90 95

Gly Val Ala Val Pro Tyr Trp Glu Trp Thr Ala Pro Ile Asp His Leu
100 105 110

Pro His Phe Ile Asp Asp Ala Thr Tyr Phe Asn Ser Arg Gln Gln Arg
115 120 125

Tyr Asp Pro Asn Pro Phe Phe Arg Gly Lys Val Thr Phe Glu Asn Ala
130 135 140

Val Thr Thr Arg Asp Pro Gln Ala Gly Leu Phe Asn Ser Asp Tyr Met
145 150 155 160

Tyr Glu Asn Val Leu Leu Ala Leu Glu Gln Glu Asn Tyr Cys Asp Phe
165 170 175

Glu Ile Gln Phe Glu Leu Val His Asn Ala Leu His Ser Met Leu Gly
180 185 190

Gly Lys Gly Gln Tyr Ser Met Ser Ser Leu Asp Tyr Ser Ala Phe Asp
195 200 205

Pro Val Phe Phe Leu His His Ala Asn Thr Asp Arg Leu Trp Ala Ile
210 215 220

Trp Gln Glu Leu Gln Arg Phe Arg Glu Leu Pro Tyr Glu Glu Ala Asn
225 230 235 240

Cys Ala Ile Asn Leu Met His Gln Pro Leu Lys Pro Phe Ser Asp Pro
245 250 255

His Glu Asn His Asp Asn Val Thr Leu Lys Tyr Ser Lys Pro Gln Asp
260 265 270

Gly Phe Asp Tyr Gln Asn His Phe Gly Tyr Lys Tyr Asp Asn Leu Glu
275 280 285

Phe His His Leu Ser Ile Pro Ser Leu Asp Ala Thr Leu Lys Gln Arg
290 295 300

Arg Asn His Asp Arg Val Phe Ala Gly Phe Leu Leu His Asn Ile Gly
305 310 315 320

Thr Ser Ala Asp Ile Thr Ile Tyr Ile Cys Leu Pro Asp Gly Arg Arg
325 330 335

Gly Asn Asp Cys Ser His Glu Ala Gly Thr Phe Tyr Ile Leu Gly Gly
340 345 350

Glu Thr Glu Met Pro Phe Ile Phe Asp Arg Leu Tyr Lys Phe Glu Ile
355 360 365

Thr Lys Pro Leu Gln Gln Leu Gly Val Lys Leu His Gly Gly Val Phe
370 375 380

Glu Leu Glu Leu Glu Ile Lys Ala Tyr Asn Gly Ser Tyr Leu Asp Pro
385 390 395 400

His Thr Phe Asp Pro Thr Ile Ile Phe Glu Pro Gly Thr
405 410

<210> 29

<211> 420

<212> PRT

<213> Haliotis tuberculata

<400> 29

Asp Thr His Ile Leu Asp His Asp His Glu Glu Glu Ile Leu Val Arg
1 5 10 15

Lys Asn Ile Ile Asp Leu Ser Pro Arg Glu Arg Val Ser Leu Val Lys
20 25 30

Ala Leu Gln Arg Met Lys Asn Asp Arg Ser Ala Asp Gly Tyr Gln Ala
35 40 45

Ile Ala Ser Phe His Ala Leu Pro Pro Leu Cys Pro Asn Pro Ser Ala
50 55 60

Ala His Arg Tyr Ala Cys Cys Val His Gly Met Ala Thr Phe Pro Gln
65 70 75 80

Trp His Arg Leu Tyr Thr Val Gln Val Gln Asp Ala Leu Arg Arg His
85 90 95

Gly Ser Leu Val Gly Ile Pro Tyr Trp Asp Trp Thr Lys Pro Val Asn
100 105 110

Glu Leu Pro Glu Leu Leu Ser Ser Ala Thr Phe Tyr His Pro Ile Arg
115 120 125

Asn Ile Asn Ile Ser Asn Pro Phe Leu Gly Ala Asp Ile Glu Phe Glu
130 135 140

Gly Pro Gly Val His Thr Glu Arg His Ile Asn Thr Glu Arg Leu Phe
145 150 155 160

His Ser Gly Asp His Asp Gly Tyr His Asn Trp Phe Phe Glu Thr Val
165 170 175

Leu Phe Ala Leu Glu Gln Glu Asp Tyr Cys Asp Phe Glu Ile Gln Phe
180 185 190

Glu Ile Ala His Asn Gly Ile His Thr Trp Ile Gly Gly Ser Ala Val
195 200 205

19

Tyr Gly Met Gly His Leu His Tyr Ala Ser Tyr Asp Pro Ile Phe Tyr
 210 215 220

Ile His His Ser Gln Thr Asp Arg Ile Trp Ala Ile Trp Gln Glu Leu
 225 230 235 240

Gln Lys Tyr Arg Gly Leu Ser Gly Ser Glu Ala Asn Cys Ala Ile Glu
 245 250 255

His Met Arg Thr Pro Leu Lys Pro Phe Ser Phe Gly Pro Pro Tyr Asn
 260 265 270

Leu Asn Ser His Thr Gln Glu Tyr Ser Lys Pro Glu Asp Thr Phe Asp
 275 280 285

Tyr Lys Lys Phe Gly Tyr Arg Tyr Asp Ser Leu Glu Leu Glu Gly Arg
 290 295 300

Ser Ile Ser Arg Ile Asp Glu Leu Ile Gln Gln Arg Gln Glu Lys Asp
 305 310 315 320

Arg Thr Phe Ala Gly Phe Leu Leu Lys Gly Phe Gly Thr Ser Ala Ser
 325 330 335

Val Ser Leu Gln Val Cys Arg Val Asp His Thr Cys Lys Asp Ala Gly
 340 345 350

Tyr Phe Thr Ile Leu Gly Gly Ser Ala Glu Met Pro Trp Ala Phe Asp
 355 360 365

Arg Leu Tyr Lys Tyr Asp Ile Thr Lys Thr Leu His Asp Met Asn Leu
 370 375 380

Arg His Glu Asp Thr Phe Ser Ile Asp Val Thr Ile Thr Ser Tyr Asn
 385 390 395 400

Gly Thr Val Leu Ser Gly Asp Leu Ile Gln Thr Pro Ser Ile Ile Phe
 405 410 415

Val Pro Gly Arg
 420

<210> 30
 <211> 417
 <212> PRT
 <213> Haliotis tuberculata

<400> 30
 His Lys Leu Asn Ser Arg Lys His Thr Pro Asn Arg Val Arg His Glu
 1 5 10 15

Leu Ser Ser Leu Ser Ser Arg Asp Ile Ala Ser Leu Lys Ala Ala Leu
 20 25 30

Thr Ser Leu Gln His Asp Asn Gly Thr Asp Gly Tyr Gln Ala Ile Ala
 35 40 45

Gln Val Leu Leu Ala Leu Glu Gln Thr Asp Phe Cys Lys Phe Glu Val
165 170 175

22


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<400> 33
His Arg Leu Phe Val Thr Gln Val Glu Asp Ala Leu Ile Arg Arg Gly
  1          5          10          15
Ser Pro Ile Gly Val Pro Tyr Trp Asp Trp Thr Gln Pro Met Ala His
          20          25          30
Leu Pro Gly Leu Ala Asp Asn Ala Thr Tyr Arg Asp Pro Ile Ser Gly
          35          40          45
Asp Ser Arg His Asn Pro Phe His Asp Val Glu Val Ala Phe Glu Asn
          50          55          60
Gly Arg Thr Glu Arg His Pro Asp Ser Arg Leu Phe Glu Gln Pro Leu
  65          70          75          80

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25

Phe Gly Lys His Thr Arg Leu Phe Asp Ser Ile Val Tyr Ala Phe Glu
85 90 95

Gln Glu Asp Phe Cys Asp Phe Glu Val Gln Phe Glu Met Thr His Asn
100 105 110

Asn Ile His Ala Trp Ile Gly Gly Gly Glu Lys Tyr Ser Met Ser Ser
115 120 125

Leu His Tyr Thr Ala Phe Asp Pro Ile Phe Tyr Leu Arg His Ser Asn
130 135 140

Thr Asp Arg Leu Trp Ala Ile Trp Gln Ala Leu Gln Ile Arg Arg Asn
145 150 155 160

Arg Pro Tyr Lys Ala His Cys Ala Trp Ser Glu Glu Arg Gln Pro Leu
165 170 175

Lys Pro Phe Ala Phe Ser Ser Pro Leu Asn Asn Asn Glu Lys Thr Tyr
180 185 190

Glu Asn Ser Val Pro Thr Asn Val Tyr Asp Tyr Glu Gly Val Leu Gly
195 200 205

Tyr Thr Tyr Asp Asp Leu Asn Phe Gly Gly Met Asp Leu Gly Gln Leu
210 215 220

Glu Glu Tyr Ile Gln Arg Gln Arg Gln Arg Asp Arg Thr Phe Ala Gly
225 230 235 240

Phe Phe Leu Ser His Ile Gly Thr Ser Ala Asn Val Glu Ile Ile Ile
245 250 255

Asp His Gly Thr Leu His Thr Ser Val Gly Thr Phe Ala Val Leu Gly
260 265 270

Gly Glu Lys Glu Met Lys Trp Gly Phe Asp Arg Leu Tyr Lys Tyr Glu
275 280 285

Ile Thr Asp Glu Leu Arg Gln Leu Asn Leu Arg Ala Asp Asp Val Phe
290 295 300

Ser Ile Ser Val Lys Val Thr Asp Val Asp Gly Ser Glu Leu Ser Ser
305 310 315 320

Glu Leu Ile Pro Ser Ala Ala Ile Ile Phe Glu Arg Ser His
325 330

<210> 34

<211> 417

<212> PRT

<213> Haliotis tuberculata

<400> 34

Ile Asp His Gln Asp Pro His His Asp Thr Ile Ile Arg Lys Asn Val
1 5 10 15

Gly Phe Leu Leu His Gly Ile Gln Gln Ser Ala Leu Val Lys Phe Phe
325 330 335

Val	Cys	Lys	Ser	Asp	Asp	Asp	Cys	Asp	His	Tyr	Ala	Gly	Glu	Phe	Tyr
			340					345					350		

Ile Leu Gly Asp Glu Ala Glu Met Pro Trp Gly Tyr Asp Arg Leu Tyr
355 360 365

Lys Tyr Glu Ile Thr Glu Gln Leu Asn Ala Leu Asp Leu His Ile Gly
370 375 380

Asp Arg Phe Phe Ile Arg Tyr Glu Ala Phe Asp Leu His Gly Thr Ser
385 390 395 400

Leu Gly Ser Asn Ile Phe Pro Lys Pro Ser Val Ile His Asp Glu Gly
405 410 415

Ala

<210> 35

<211> 415

<212> PRT

<213> *Haliotis tuberculata*

<400> 35

Gly His His Gln Ala Asp Glu Tyr Asp Glu Val Val Thr Ala Ala Ser
1 5 10 15

His Ile Arg Lys Asn Leu Lys Asp Leu Ser Lys Gly Glu Val Glu Ser
20 25 30

Leu Arg Ser Ala Phe Leu Gln Leu Gln Asn Asp Gly Val Tyr Glu Asn
35 40 45

Ile Ala Lys Phe His Gly Lys Pro Gly Leu Cys Asp Asp Asn Gly Arg
50 55 60

Lys Val Ala Cys Cys Val His Gly Met Pro Thr Phe Pro Gln Trp His
65 70 75 80

Arg Leu Tyr Val Leu Gln Val Glu Asn Ala Leu Leu Glu Arg Gly Ser
85 90 95

Ala Val Ser Val Pro Tyr Trp Asp Trp Thr Glu Thr Phe Thr Glu Leu
100 105 110

Pro Ser Leu Ile Ala Glu Ala Thr Tyr Phe Asn Ser Arg Gln Gln Thr
115 120 125

Phe Asp Pro Asn Pro Phe Phe Arg Gly Lys Ile Ser Phe Glu Asn Ala
130 135 140

<400> 36

Ser	Phe	Leu	Arg	Pro	Asp	Gly	His	Ser	Asp	Asp	Ile	Leu	Val	Arg	Lys
1				5					10					15	
Glu	Val	Asn	Ser	Leu	Thr	Thr	Arg	Glu	Thr	Ala	Ser	Leu	Ile	His	Ala
			20					25					30		
Leu	Lys	Ser	Met	Gln	Glu	Asp	His	Ser	Pro	Asp	Gly	Phe	Gln	Ala	Ile
		35					40					45			
Ala	Ser	Phe	His	Ala	Leu	Pro	Pro	Leu	Cys	Pro	Ser	Pro	Ser	Ala	Ala
	50					55					60				
His	Arg	Tyr	Ala	Cys	Cys	Val	His	Gly	Met	Ala	Thr	Phe	Pro	Gln	Trp
65					70					75					80
His	Arg	Leu	Tyr	Thr	Val	Gln	Phe	Gln	Asp	Ala	Leu	Arg	Arg	His	Gly
				85					90					95	
Ala	Thr	Val	Gly	Val	Pro	Tyr	Trp	Asp	Trp	Leu	Arg	Pro	Gln	Ser	His
			100					105					110		
Leu	Pro	Glu	Leu	Val	Thr	Met	Glu	Thr	Tyr	His	Asp	Ile	Trp	Ser	Asn
		115					120					125			
Arg	Asp	Phe	Pro	Asn	Pro	Phe	Tyr	Gln	Ala	Asn	Ile	Glu	Phe	Glu	Gly
	130					135					140				
Glu	Asn	Ile	Thr	Thr	Glu	Arg	Glu	Val	Ile	Ala	Asp	Lys	Leu	Phe	Val
145					150					155					160
Lys	Gly	Gly	His	Val	Phe	Asp	Lys	Leu	Val	Leu	Gln	Thr	Ser	His	Pro
				165					170					175	
Ser	Ala	Glu	Gln	Glu	Asn	Tyr	Cys	Asp	Phe	Glu	Ile	Gln	Phe	Glu	Ile
			180					185					190		
Leu	His	Asn	Gly	Val	His	Thr	Trp	Val	Gly	Gly	Ser	Arg	Thr	Tyr	Ser
		195					200					205			
Ile	Gly	His	Leu	His	Tyr	Ala	Phe	Tyr	Asp	Pro	Leu	Phe	Tyr	Leu	His
	210					215					220				
His	Phe	Gln	Thr	Asp	Arg	Ile	Trp	Ala	Ile	Trp	Gln	Glu	Leu	Gln	Glu
225					230					235					240
Gln	Arg	Gly	Leu	Ser	Gly	Asp	Glu	Ala	His	Cys	Ala	Leu	Glu	Gln	Met
				245					250					255	
Arg	Glu	Pro	Leu	Lys	Pro	Phe	Ser	Phe	Gly	Ala	Pro	Tyr	Asn	Trp	Asn
			260					265					270		
Gln	Leu	Thr	Gln	Asp	Phe	Ser	Arg	Pro	Glu	Asp	Thr	Phe	Asp	Tyr	Arg
		275					280					285			
Lys	Phe	Gly	Tyr	Glu	Tyr	Asp	Asn	Leu	Glu	Phe	Leu	Gly	Met	Ser	Val
	290					295					300				

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<400> 37
Arg Asp Ile Asn Thr Arg Ser Met Ser Pro Asn Arg Val Arg Arg Glu
 1          5          10          15
Leu Ser Asp Leu Ser Ala Arg Asp Leu Ser Ser Leu Lys Ser Ala Leu
      20          25          30
Arg Asp Leu Gln Glu Asp Asp Gly Pro Asn Gly Tyr Gln Ala Leu Ala
      35          40          45
Ala Phe His Gly Leu Pro Ala Gly Cys His Asp Ser Arg Gly Asn Glu
      50          55          60
Ile Ala Cys Cys Ile His Gly Met Pro Thr Phe Pro Gln Trp His Arg
 65          70          75          80
Leu Tyr Thr Leu Gln Leu Glu Met Ala Leu Arg Arg His Gly Ser Ser
      85          90          95
Val Ala Ile Pro Tyr Trp Asp Trp Thr Lys Pro Ile Ser Glu Leu Pro
      100          105          110
Ser Leu Phe Thr Ser Pro Glu Tyr Tyr Asp Pro Trp His Asp Ala Val
      115          120          125

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Val	Asn	Asn	Pro	Phe	Ser	Lys	Gly	Phe	Val	Lys	Phe	Ala	Asn	Thr	Tyr
130						135					140				
Thr	Val	Arg	Asp	Pro	Gln	Glu	Met	Leu	Phe	Gln	Leu	Cys	Glu	His	Gly
145					150					155					160
Glu	Ser	Ile	Leu	Tyr	Glu	Gln	Thr	Leu	Leu	Ala	Leu	Glu	Gln	Thr	Asp
				165					170					175	
Tyr	Cys	Asp	Phe	Glu	Val	Gln	Phe	Glu	Val	Leu	His	Asn	Val	Ile	His
			180					185					190		
Tyr	Leu	Val	Gly	Gly	Arg	Gln	Thr	Tyr	Ala	Leu	Ser	Ser	Leu	His	Tyr
		195					200					205			
Ala	Ser	Tyr	Asp	Pro	Phe	Phe	Phe	Ile	His	His	Ser	Phe	Val	Asp	Lys
	210					215						220			
Met	Trp	Val	Val	Trp	Gln	Ala	Leu	Gln	Lys	Arg	Arg	Lys	Leu	Pro	Tyr
225					230					235					240
Lys	Arg	Ala	Asp	Cys	Ala	Val	Asn	Leu	Met	Thr	Lys	Pro	Met	Arg	Pro
				245					250					255	
Phe	Asp	Ser	Asp	Met	Asn	Gln	Asn	Pro	Phe	Thr	Lys	Met	His	Ala	Val
			260					265					270		
Pro	Asn	Thr	Leu	Tyr	Asp	Tyr	Glu	Thr	Leu	Tyr	Tyr	Ser	Tyr	Asp	Asn
		275					280					285			
Leu	Glu	Ile	Gly	Gly	Arg	Asn	Leu	Asp	Gln	Leu	Gln	Ala	Glu	Ile	Asp
	290					295					300				
Arg	Ser	Arg	Ser	His	Asp	Arg	Val	Phe	Ala	Gly	Phe	Leu	Leu	Arg	Gly
305					310					315					320
Ile	Gly	Thr	Ser	Ala	Asp	Val	Arg	Phe	Trp	Ile	Cys	Arg	Asn	Glu	Asn
				325					330					335	
Asp	Cys	His	Arg	Gly	Gly	Ile	Ile	Phe	Ile	Leu	Gly	Gly	Ala	Lys	Glu
			340					345					350		
Met	Pro	Trp	Ser	Phe	Asp	Arg	Asn	Phe	Lys	Phe	Asp	Ile	Thr	His	Val
		355					360					365			
Leu	Glu	Asn	Ala	Gly	Ile	Ser	Pro	Glu	Asp	Val	Phe	Asp	Ala	Glu	Glu
	370					375					380				
Pro	Phe	Tyr	Ile	Lys	Val	Glu	Ile	His	Ala	Val	Asn	Lys	Thr	Met	Ile
385					390					395					400
Pro	Ser	Ser	Val	Ile	Pro	Ala	Pro	Thr	Ile	Ile	Tyr	Ser	Pro	Gly	Glu
				405					410					415	

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<210> 38
<211> 402
<212> PRT
<213> Haliotis tuberculata
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<400> 38

Gly Arg Ala Ala Asp Ser Ala His Ser Ala Asn Ile Ala Gly Ser Gly
1 5 10 15

Val Arg Lys Asp Val Thr Thr Leu Thr Val Ser Glu Thr Glu Asn Leu
20 25 30

Arg Gln Ala Leu Gln Gly Val Ile Asp Asp Thr Gly Pro Asn Gly Tyr
35 40 45

Gln Ala Ile Ala Ser Phe His Gly Ser Pro Pro Met Cys Glu Met Asn
50 55 60

Gly Arg Lys Val Ala Cys Cys Ala His Gly Met Ala Ser Phe Pro His
65 70 75 80

Trp His Arg Leu Tyr Val Lys Gln Met Glu Asp Ala Leu Ala Asp His
85 90 95

Gly Ser His Ile Gly Ile Pro Tyr Trp Asp Trp Thr Thr Ala Phe Thr
100 105 110

Glu Leu Pro Ala Leu Val Thr Asp Ser Glu Asn Asn Pro Phe His Glu
115 120 125

Gly Arg Ile Asp His Leu Gly Val Thr Thr Ser Arg Ser Pro Arg Asp
130 135 140

Met Leu Phe Asn Asp Pro Glu Gln Gly Ser Glu Ser Phe Phe Tyr Arg
145 150 155 160

Gln Val Leu Leu Ala Leu Glu Gln Thr Asp Tyr Cys Gln Phe Glu Val
165 170 175

Gln Phe Glu Leu Thr His Asn Ala Ile His Ser Trp Thr Gly Gly Arg
180 185 190

Ser Pro Tyr Gly Met Ser Thr Leu Glu Phe Thr Ala Tyr Asp Pro Leu
195 200 205

Phe Trp Leu His His Ser Asn Thr Asp Arg Ile Trp Ala Val Trp Gln
210 215 220

Ala Leu Gln Lys Tyr Arg Gly Leu Pro Tyr Asn Glu Ala His Cys Glu
225 230 235 240

Ile Gln Val Leu Lys Gln Pro Leu Arg Pro Phe Asn Asp Asp Ile Asn
245 250 255

His Asn Pro Ile Thr Lys Thr Asn Ala Arg Pro Ile Asp Ser Phe Asp
260 265 270

33

Tyr Glu Arg Phe Asn Tyr Gln Tyr Asp Thr Leu Ser Phe His Gly Lys
 275 280 285

Ser Ile Pro Glu Leu Asn Asp Leu Leu Glu Glu Arg Lys Arg Glu Glu
 290 295 300

Arg Thr Phe Ala Ala Phe Leu Leu Arg Gly Ile Gly Cys Ser Ala Asp
 305 310 315 320

Val Val Phe Asp Ile Cys Arg Pro Asn Gly Asp Cys Val Phe Ala Gly
 325 330 335

Thr Phe Ala Val Leu Gly Gly Glu Leu Glu Met Pro Trp Ser Phe Asp
 340 345 350

Arg Leu Phe Arg Tyr Asp Ile Thr Arg Val Met Asn Gln Leu His Leu
 355 360 365

Gln Tyr Asp Ser Asp Phe Ser Phe Arg Val Lys Leu Val Ala Thr Asn
 370 375 380

Gly Thr Glu Leu Ser Ser Asp Leu Leu Lys Ser Pro Thr Ile Glu His
 385 390 395 400

Glu Leu

<210> 39
 <211> 515
 <212> PRT
 <213> *Haliotis tuberculata*

<400> 39
 Gly Ala His Arg Gly Pro Val Glu Glu Thr Glu Val Thr Arg Gln His
 1 5 10 15

Thr Asp Gly Asn Ala His Phe His Arg Lys Glu Val Asp Ser Leu Ser
 20 25 30

Leu Asp Glu Ala Asn Asn Leu Lys Asn Ala Leu Tyr Lys Leu Gln Asn
 35 40 45

Asp His Ser Leu Thr Gly Tyr Glu Ala Ile Ser Gly Tyr His Gly Tyr
 50 55 60

Pro Asn Leu Cys Pro Glu Glu Gly Asp Asp Lys Ile Pro Leu Leu Arg
 65 70 75 80

Pro Arg Met Gly Ile Phe Pro Tyr Trp His Arg Leu Leu Thr Ile Gln
 85 90 95

Leu Glu Arg Ala Leu Glu His Asn Gly Ala Leu Leu Gly Val Pro Tyr
 100 105 110

34

Trp	Asp	Trp	Asn	Lys	Asp	Leu	Ser	Ser	Leu	Pro	Ala	Phe	Phe	Ser	Asp	
		115					120					125				
Ser	Ser	Asn	Asn	Asn	Pro	Tyr	Phe	Lys	Tyr	His	Ile	Ala	Gly	Val	Gly	
	130					135					140					
His	Asp	Thr	Val	Arg	Glu	Pro	Thr	Ser	Leu	Ile	Tyr	Asn	Gln	Pro	Gln	
145					150					155					160	
Ile	His	Gly	Tyr	Asp	Tyr	Leu	Tyr	Tyr	Leu	Ala	Leu	Thr	Thr	Leu	Glu	
				165					170						175	
Glu	Asn	Asn	Tyr	Trp	Asp	Phe	Glu	Val	Gln	Tyr	Glu	Ile	Leu	His	Asn	
			180					185					190			
Ala	Val	His	Ser	Trp	Leu	Gly	Gly	Ser	Gln	Lys	Tyr	Ser	Met	Ser	Thr	
		195					200					205				
Leu	Glu	Tyr	Ser	Ala	Phe	Asp	Pro	Val	Phe	Met	Ile	Leu	His	Ser	Gly	
	210					215					220					
Leu	Asp	Arg	Leu	Trp	Ile	Ile	Trp	Gln	Glu	Leu	Gln	Lys	Ile	Arg	Arg	
225					230					235					240	
Lys	Pro	Tyr	Asn	Phe	Ala	Lys	Cys	Ala	Tyr	His	Met	Met	Glu	Glu	Pro	
				245					250					255		
Leu	Ala	Pro	Phe	Ser	Tyr	Pro	Ser	Ile	Asn	Gln	Asp	Glu	Phe	Thr	Arg	
			260					265					270			
Ala	Asn	Ser	Lys	Pro	Ser	Thr	Val	Phe	Asp	Ser	His	Lys	Phe	Gly	Tyr	
		275					280					285				
His	Tyr	Asp	Asn	Leu	Asn	Val	Arg	Gly	His	Ser	Ile	Gln	Glu	Leu	Asn	
	290					295					300					
Thr	Ile	Ile	Asn	Asp	Leu	Arg	Asn	Thr	Asp	Arg	Ile	Tyr	Ala	Gly	Phe	
305					310					315					320	
Val	Leu	Ser	Gly	Ile	Gly	Thr	Ser	Ala	Ser	Val	Lys	Ile	Tyr	Leu	Arg	
				325					330					335		
Thr	Asp	Asp	Asn	Asp	Glu	Glu	Val	Gly	Thr	Phe	Thr	Val	Leu	Gly	Gly	
			340					345					350			
Glu	Arg	Glu	Met	Pro	Trp	Ala	Tyr	Glu	Arg	Val	Phe	Lys	Tyr	Asp	Ile	
		355					360					365				
Thr	Glu	Val	Ala	Asp	Arg	Leu	Lys	Ile	Lys	Leu	Trp	Gly	His	Pro	Leu	
	370					375					380					
Thr	Ser	Gly	Thr	Gly	Asp	His	Ile	Leu	Thr	Asn	Gly	Ile	Gly	Gly	Lys	
385					390					395					400	
Gln	Glu	Pro	Thr	Gln	Ile	Leu	Ser	Ser	Ser	Thr	Asp	Leu	Pro	Ile	Met	
				405					410					415		

Tyr Arg Ala His Cys Ala Ile Ser Leu Glu His Met His Leu Lys Pro
145 150 155 160

38

```

<400> 43
Asp Ser Ala His Thr Asp Asp Gly His Thr Glu Pro Val Met Ile Arg
  1          5          10          15
Lys Asp Ile Thr Gln Leu Asp Lys Arg Gln Gln Leu Ser Leu Val Lys
          20          25          30
Ala Leu Glu Ser Met Lys Ala Asp His Ser Ser Asp Gly Phe Gln Ala
          35          40          45
Ile Ala Ser Phe His Ala Leu Pro Pro Leu Cys Pro Ser Pro Ala Ala
  50          55          60
Ser Lys Arg Phe Ala Cys Cys Val His Gly Met Pro Thr Phe Pro Gln
  65          70          75          80

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Ser Tyr Ile Gly Thr Ser Ala Ser Val Asp Ile Phe Ile Asn Arg Glu
225 230 235 240

<400> 45															
Asp	Ala	Lys	Asp	Phe	Gly	His	Ser	Arg	Lys	Ile	Arg	Lys	Ala	Val	Asp
1				5					10					15	
Ser	Leu	Thr	Val	Glu	Glu	Gln	Thr	Ser	Leu	Arg	Arg	Ala	Met	Ala	Asp
			20					25					30		
Leu	Gln	Asp	Asp	Lys	Thr	Ser	Gly	Gly	Phe	Gln	Gln	Ile	Ala	Ala	Phe
		35					40					45			
His	Gly	Glu	Pro	Lys	Trp	Cys	Pro	Ser	Pro	Glu	Ala	Glu	Lys	Lys	Phe
	50					55					60				
Ala	Cys	Cys	Val	His	Gly	Met	Ala	Val	Phe	Pro	His	Trp	His	Arg	Leu
65					70					75					80
Leu	Thr	Val	Gln	Gly	Glu	Asn	Ala	Leu	Arg	Lys	His	Gly	Phe	Thr	Gly
				85					90					95	
Gly	Leu	Pro	Tyr	Trp	Asp	Trp	Thr	Arg	Ser	Met	Ser	Ala	Leu	Pro	His
			100					105					110		
Phe	Val	Ala	Asp	Pro	Thr	Tyr	Asn	Asp	Ala	Ile	Ser	Ser	Gln	Glu	Glu
		115					120					125			
Asp	Asn	Pro	Trp	His	His	Gly	His	Ile	Asp	Ser	Val	Gly	His	Asp	Thr
	130					135					140				
Thr	Arg	Asp	Val	Arg	Asp	Asp	Leu	Tyr	Gln	Ser	Pro	Gly	Phe	Gly	His
145					150					155					160
Tyr	Thr	Asp	Ile	Ala	Gln	Gln	Val	Leu	Leu	Ala	Phe	Glu	Gln	Asp	Ser
				165					170					175	

<400> 46
Gly Ser His Gln Ala Asp Glu Tyr Arg Glu Ala Val Thr Ser Ala Ser
1 5 10 15
His Ile Arg Lys Asn Ile Arg Asp Leu Ser Glu Gly Glu Ile Glu Ser
20 25 30

43

Ile Arg Ser Ala Phe Leu Gln Ile Gln Lys Glu Gly Ile Tyr Glu Asn
 35 40 45
 Ile Ala Lys Phe His Gly Lys Pro Gly Leu Cys Glu His Asp Gly His
 50 55 60
 Pro Val Ala Cys Cys Val His Gly Met Pro Thr Phe Pro His Trp His
 65 70 75 80
 Arg Leu Tyr Val Leu Gln Val Glu Asn Ala Leu Leu Glu Arg Gly Ser
 85 90 95
 Ala Val Ala Val Pro Tyr Trp Asp Trp Thr Leu Pro Arg
 100 105

<210> 47
 <211> 329
 <212> PRT
 <213> Megathura crenulata

<400> 47
 Met Ala Val Phe Pro His Trp His Arg Leu Phe Val Lys Gln Met Glu
 1 5 10 15
 Asp Ala Leu Ala Ala His Gly Ala His Ile Gly Ile Pro Tyr Trp Asp
 20 25 30
 Trp Thr Ser Ala Phe Ser His Leu Pro Ala Leu Val Thr Asp His Glu
 35 40 45
 Asn Asn Pro Phe His His Gly His Ile Gly His Leu Asn Val Asp Thr
 50 55 60
 Ser Arg Ser Pro Arg Asp Met Leu Phe Asn Asp Pro Glu Gln Gly Ser
 65 70 75 80
 Glu Ser Phe Phe Tyr Arg Gln Val Leu Leu Thr Leu Glu Gln Thr Asp
 85 90 95
 Phe Cys Gln Phe Glu Val Gln Phe Glu Leu Thr His Asn Ala Ile His
 100 105 110
 Ser Trp Thr Gly Gly His Thr Pro Tyr Gly Met Ser Ser Leu Glu Tyr
 115 120 125
 Thr Ala Tyr Asp Pro Leu Phe Tyr Leu His His Ser Asn Thr Asp Arg
 130 135 140
 Ile Trp Ala Ile Trp Gln Ala Leu Gln Lys Tyr Arg Gly Leu Pro Tyr
 145 150 155 160
 Asn Ala Ala His Cys Asp Ile Gln Val Leu Lys Gln Pro Leu Lys Pro
 165 170 175

[illegible]


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<210> 49
<211> 1269
<212> DNA
<213> Haliotis tuberculata
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<400>	49						
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gaaaggacgt	gagtcacctc	acggatgacg	aggtgcaagc	tctccacggc	gccctccatg	120	
acgtcactgc	atctacaggg	cctctgagtt	tccaagacat	aacatcttac	catgccgcac	180	
cagcgtcgtg	tgactacaag	ggacggaaga	tgccttgctg	tgtccacggg	atgccaggtt	240	
tccccttctg	gcacagggca	tatgtcgtcc	aagccgagcg	ggcactgttg	tccaaacgga	300	
agactgtcgg	aatgccttac	tgggactgga	cgcaaacgct	gactcactta	ccatctcttg	360	
tgactgaacc	catctacatt	gacagtaaag	gtggaaaggc	tcaaaccaac	tactggtacc	420	
gcggcgagat	agcgttcatt	aataagaaga	ctgcgcgagc	tgtagatgat	cgcctattcg	480	
agaagggtgga	gcctggtcac	tacacacatc	ttatggagac	tgtcctcgac	gctctcgaac	540	
aggacgaatt	ctgtaaattt	gaaatccagt	tcgagttggc	tcataatgct	atccattact	600	
tggttggcgg	taaatttgaa	tattcaatgt	caaacttgga	atacacctcc	tacgacccca	660	
tcttcttctt	ccaccactcc	aacgttgacc	gcctcttcgc	catctggcag	cgtcttcagg	720	
aactgcgagg	aaagaatccc	aatgcaatgg	actgtgcaca	tgaactcgct	caccagcaac	780	
tccaaccctt	caacagggac	agcaatccag	tccagctcac	aaaggaccac	tgcacacctg	840	
ctgacctctt	tgattacaaa	caacttggat	acagctacga	cagcttaaac	ctgaatggaa	900	
tgacgccaga	acagctgaaa	acagaactag	acgaacgcca	ctccaaagaa	cgtgcgtttg	960	
caagcttccg	actcagtggc	tttggggggt	ctgccaaagt	tgttgtctat	gcatgtgtcc	1020	
ctgatgatga	tccacgcagt	gatgactact	gcgagaaaagc	aggcgacttc	ttcattcttg	1080	
gggggtcaaag	cgaaatgccg	tggagattct	acgaccctt	cttctatgat	gtaactgaag	1140	
cgggtacatca	ccttggagtc	cggctaagtg	gcgactacta	tgtgaaaaca	gaactcttca	1200	
gcgtgaatgg	cacagcaatt	tcacctgata	ttcttctctca	accaactgtt	gcctaccgac	1260	
ctgggaaag						1269	

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<210> 50
<211> 569
<212> DNA
<213> Haliotis tuberculata
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<400> 50						
ggtcttccgt	actgggactg	gacgcagcat	ctgactcaac	tcccagatct	ggtgtcagac	60
cccttgtttg	tcgacccgga	aggaggaaag	gcccatgaca	acgcattgta	tcgtggaaac	120
atcaagtttg	agaataagaa	gactgcaaga	gctgttgacg	atcgctttt	cgagaagggt	180
ggaccaggag	agaatacccg	actctttgaa	ggaattctcg	atgctcttga	acaggatgaa	240
ttctgcaact	tcgagatcca	gtttgagttg	gctcacaacg	ctatccacta	cctgggtggc	300
ggccgtcaca	cgtactccat	gtctcatctc	gagttacacc	ctcctacgac	cccctcttct	360
tcctccatca	ctccaacacc	ggaccgcate	ttcgccatct	gggaaagctc	tcagggtactc	420
agaggaatag	acccaacac	cgccgactgc	gcacacaacc	tcattccatga	gcccatggaa	480
ccgttccgct	gggaactcgaa	cctcttgac	ctcaccaggg	aaaactccaa	accaattgac	540
agctttgatt	atgcccacct	tggctacca				569

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<210> 51
<211> 1246
<212> DNA
<213> Haliotis tuberculata
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<400> 51
gttacagagg cccagctcc ctctcggat gctcacctcg ccgtcaggaa ggatatcaac 60
catctgacac gcgaggaggt gtacgagctg cgcagagcta tggagagatt ccaggccgac 120
acatccgttg atgggtacca ggctacggtt gagtatcacg gcttacctgc tcgatqtcca 180

46

ttccccgagg	ccacaaatag	gttcgcctgt	tgcattccacg	gcattggcgac	attccctcat	240
tggcacagac	tgttcgtcac	ccaggtggaa	gatgctctga	tcaggcgagg	atcgccata	300
gggggtccct	actgggactg	gactcagcct	atggcgcatc	tcccaggact	tgcagacaac	360
gccacctata	gagatcccat	cagcggggac	agcagacaca	accccttcca	cgatgttgaa	420
gttgcccttg	aaaatggacg	tacagaacgt	caccagata	gtagattgtt	tgaacaacct	480
ttatttggca	aacatacgcg	tctcttcgac	agtatagtct	atgcttttga	gcaggaggac	540
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ggcggcgaga	agtattccat	gtcttctcta	cactacacag	ccttcgaccc	tatcttctac	660
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<211> 1242

<212> DNA

<213> *Haliotis tuberculata*

<400> 52

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<211> 1257

<212> DNA

<213> *Haliotis tuberculata*

<400> 53

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47

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<211> 1257

<212> DNA

<213> Megathura crenulata

<400> 54

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<211> 1254

<212> DNA

<213> Megathura crenulata

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48

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<211> 509

<212> DNA

<213> Megathura crenulata

<400> 56

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<212> DNA

<213> Megathura crenulata

<400> 57

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56

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His	Leu	Pro	Gly	Leu	Ala	Asp	Asn	Ala	Thr	Tyr	Arg	Asp	Pro	Ile	Ser
		115					120					125			
Gly	Asp	Ser	Arg	His	Asn	Pro	Phe	His	Asp	Val	Glu	Val	Ala	Phe	Glu
	130					135					140				
Asn	Gly	Arg	Thr	Glu	Arg	His	Pro	Asp	Ser	Arg	Leu	Phe	Glu	Gln	Pro
	145				150					155					160
Leu	Phe	Gly	Lys	His	Thr	Arg	Leu	Phe	Asp	Ser	Ile	Val	Tyr	Ala	Phe
				165					170					175	
Glu	Gln	Glu	Asp	Phe	Cys	Asp	Phe	Glu	Val	Gln	Phe	Glu	Met	Thr	His
			180					185					190		
Asn	Asn	Ile	His	Ala	Trp	Ile	Gly	Gly	Gly	Glu	Lys	Tyr	Ser	Met	Ser
		195					200					205			
Ser	Leu	His	Tyr	Thr	Ala	Phe	Asp	Pro	Ile	Phe	Tyr	Leu	Arg	His	Ser
	210					215					220				
Asn	Thr	Asp	Arg	Leu	Trp	Ala	Ile	Trp	Gln	Ala	Leu	Gln	Ile	Arg	Arg
	225				230					235					240
Asn	Arg	Pro	Tyr	Lys	Ala	His	Cys	Ala	Trp	Ser	Glu	Glu	Arg	Gln	Pro
				245					250					255	
Leu	Lys	Pro	Phe	Ala	Phe	Ser	Ser	Pro	Leu	Asn	Asn	Asn	Glu	Lys	Thr
			260					265					270		
Tyr	Glu	Asn	Ser	Val	Pro	Thr	Asn	Val	Tyr	Asp	Tyr	Glu	Gly	Val	Leu
		275					280					285			
Gly	Tyr	Thr	Tyr	Asp	Asp	Leu	Asn	Phe	Gly	Gly	Met	Asp	Leu	Gly	Gln
	290					295					300				
Leu	Glu	Glu	Tyr	Ile	Gln	Arg	Gln	Arg	Gln	Arg	Asp	Arg	Thr	Phe	Ala
	305				310					315					320
Gly	Phe	Phe	Leu	Ser	His	Ile	Gly	Thr	Ser	Ala	Asn	Val	Glu	Ile	Ile
				325					330					335	
Ile	Asp	His	Gly	Thr	Leu	His	Thr	Ser	Val	Gly	Thr	Phe	Ala	Val	Leu
			340					345					350		

Gly Arg Ala Thr Tyr Ser Ile Ser Ser Leu Asp Tyr Ser Ala Phe Asp
195 200 205

Pro Val Phe Phe Leu His His Ala Asn Thr Asp Arg Leu Trp Ala Ile
 210 215 220
 Trp Gln Glu Leu Gln Arg Tyr Arg Lys Lys Pro Tyr Asn Glu Ala Asp
 225 230 235 240
 Cys Ala Ile Asn Leu Met Arg Lys Pro Leu His Pro Phe Asp Asn Ser
 245 250 255
 Asp Leu Asn His Asp Pro Val Thr Phe Lys Tyr Ser Lys Pro Thr Asp
 260 265 270
 Gly Phe Asp Tyr Gln Asn Asn Phe Gly Tyr Lys Tyr Asp Asn Leu Glu
 275 280 285
 Phe Asn His Phe Ser Ile Pro Arg Leu Glu Glu Ile Ile Arg Ile Arg
 290 295 300
 Gln Arg Gln Asp Arg Val Phe Ala Gly Phe Leu Leu His Asn Ile Gly
 305 310 315 320
 Thr Ser Ala Thr Val Glu Ile Phe Val Cys Val Pro Thr Thr Ser Gly
 325 330 335
 Glu Gln Asn Cys Glu Asn Lys Ala Gly Thr Phe Ala Val Leu Gly Gly
 340 345 350
 Glu Thr Glu Met Ala Phe His Phe Asp Arg Leu Tyr Arg Phe Asp Ile
 355 360 365
 Ser Glu Thr Leu Arg Asp Leu Gly Ile Gln Leu Asp Ser His Asp Phe
 370 375 380
 Asp Leu Ser Ile Lys Ile Gln Gly Val Asn Gly Ser Tyr Leu Asp Pro
 385 390 395 400
 His Ile Leu Pro Glu Pro Ser Leu Ile Phe Val Pro Gly Ser
 405 410

<210> 68

<211> 419

<212> PRT

<213> *Haliotis tuberculata*

<400> 68

Ser Ser Phe Leu Arg Pro Asp Gly His Ser Asp Asp Ile Leu Val Arg
 1 5 10 15

Lys Glu Val Asn Ser Leu Thr Thr Arg Glu Thr Ala Ser Leu Ile His
 20 25 30

Ala Leu Lys Ser Met Gln Glu Asp His Ser Pro Asp Gly Phe Gln Ala
 35 40 45

60

Phe Thr Val Leu Gly Gly Ser Ala Glu Met Ala Trp Ala Phe Asp Arg
355 360 365

Leu Tyr Lys Tyr Asp Ile Thr Glu Thr Leu Glu Lys Met His Leu Arg
370 375 380

Tyr Asp Asp Asp Phe Thr Ile Ser Val Ser Leu Thr Ala Asn Asn Gly
385 390 395 400

Thr Val Leu Ser Ser Ser Leu Ile Pro Thr Pro Ser Val Ile Phe Gln
405 410 415

Arg Gly His

<210> 69

<211> 378

<212> PRT

<213> Megathura crenulata

<400> 69

Arg Tyr Gln Ala Thr Ala Glu Tyr His Gly Leu Pro Ala Arg Cys Pro
1 5 10 15

Arg Pro Asp Ala Lys Asp Arg Tyr Ala Cys Cys Val His Gly Met Pro
20 25 30

Ile Phe Pro His Trp His Arg Leu Phe Val Thr Gln Val Glu Asp Ala
35 40 45

Leu Val Gly Arg Gly Ala Thr Ile Gly Ile Pro Tyr Trp Asp Trp Thr
50 55 60

Glu Pro Met Thr His Ile Pro Gly Leu Ala Gly Asn Lys Thr Tyr Val
65 70 75 80

Asp Ser His Gly Ala Ser His Thr Asn Pro Phe His Ser Ser Val Ile
85 90 95

Ala Phe Glu Glu Asn Ala Pro His Thr Lys Arg Gln Ile Asp Gln Arg
100 105 110

Leu Phe Lys Pro Ala Thr Phe Gly His His Thr Asp Leu Phe Asn Gln
115 120 125

Ile Leu Tyr Ala Phe Glu Gln Glu Asp Tyr Cys Asp Phe Glu Val Gln
130 135 140

Phe Glu Ile Thr His Asn Thr Ile His Ala Trp Thr Gly Gly Ser Glu
145 150 155 160

His Phe Ser Met Ser Ser Leu His Tyr Thr Ala Phe Asp Pro Leu Phe
165 170 175

Tyr Phe His His Ser Asn Val Asp Arg Leu Trp Ala Val Trp Gln Ala
180 185 190

61

Leu Gln Met Arg Arg His Lys Pro Tyr Arg Ala His Cys Ala Ile Ser
195 200 205

Leu Glu His Met His Leu Lys Pro Phe Ala Phe Ser Ser Pro Leu Asn
210 215 220

Asn Asn Glu Lys Thr His Ala Asn Ala Met Pro Asn Lys Ile Tyr Asp
225 230 235 240

Tyr Glu Asn Val Leu His Tyr Thr Tyr Glu Asp Leu Thr Phe Gly Gly
245 250 255

Ile Ser Leu Glu Asn Ile Glu Lys Met Ile His Glu Asn Gln Gln Glu
260 265 270

Asp Arg Ile Tyr Ala Gly Phe Leu Leu Ala Gly Ile Arg Thr Ser Ala
275 280 285

Asn Val Asp Ile Phe Ile Lys Thr Thr Asp Ser Val Gln His Lys Ala
290 295 300

Gly Thr Phe Ala Val Leu Gly Gly Ser Lys Glu Met Lys Trp Gly Phe
305 310 315 320

Asp Arg Val Phe Lys Phe Asp Ile Thr His Val Leu Lys Asp Leu Asp
325 330 335

Leu Thr Ala Asp Gly Asp Phe Glu Val Thr Val Asp Ile Thr Glu Val
340 345 350

Asp Gly Thr Lys Leu Ala Ser Ser Leu Ile Pro His Ala Ser Val Ile
355 360 365

Arg Glu His Ala Arg Gly Lys Leu Asn Arg
370 375

<210> 70
<211> 419
<212> PRT
<213> Megathura crenulata

<400> 70
Asp Ser Ala His Thr Asp Asp Gly His Thr Glu Pro Val Met Ile Arg
1 5 10 15

Lys Asp Ile Thr Gln Leu Asp Lys Arg Gln Gln Leu Ser Leu Val Lys
20 25 30

Ala Leu Glu Ser Met Lys Ala Asp His Ser Ser Asp Gly Phe Gln Ala
35 40 45

Ile Ala Ser Phe His Ala Leu Pro Pro Leu Cys Pro Ser Pro Ala Ala
50 55 60

62

Ser	Lys	Arg	Phe	Ala	Cys	Cys	Val	His	Gly	Met	Ala	Thr	Phe	Pro	Gln	65	70	75	80
Trp	His	Arg	Leu	Tyr	Thr	Val	Gln	Phe	Gln	Asp	Ser	Leu	Arg	Lys	His	85	90	95	
Gly	Ala	Val	Val	Gly	Leu	Pro	Tyr	Trp	Asp	Trp	Thr	Leu	Pro	Arg	Ser	100	105	110	
Glu	Leu	Pro	Glu	Leu	Leu	Thr	Val	Ser	Thr	Ile	His	Asp	Pro	Glu	Thr	115	120	125	
Gly	Arg	Asp	Ile	Pro	Asn	Pro	Phe	Ile	Gly	Ser	Lys	Ile	Glu	Phe	Glu	130	135	140	
Gly	Glu	Asn	Val	His	Thr	Lys	Arg	Asp	Ile	Asn	Arg	Asp	Arg	Leu	Phe	145	150	155	160
Gln	Gly	Ser	Thr	Lys	Thr	His	His	Asn	Trp	Phe	Ile	Glu	Gln	Ala	Leu	165	170	175	
Leu	Ala	Leu	Glu	Gln	Thr	Asn	Tyr	Cys	Asp	Phe	Glu	Val	Gln	Phe	Glu	180	185	190	
Ile	Met	His	Asn	Gly	Val	His	Thr	Trp	Val	Gly	Gly	Lys	Glu	Pro	Tyr	195	200	205	
Gly	Ile	Gly	His	Leu	His	Tyr	Ala	Ser	Tyr	Asp	Pro	Leu	Phe	Tyr	Ile	210	215	220	
His	His	Ser	Gln	Thr	Asp	Arg	Ile	Trp	Ala	Ile	Trp	Gln	Ser	Leu	Gln	225	230	235	240
Arg	Phe	Arg	Gly	Leu	Ser	Gly	Ser	Glu	Ala	Asn	Cys	Ala	Val	Asn	Leu	245	250	255	
Met	Lys	Thr	Pro	Leu	Lys	Pro	Phe	Ser	Phe	Gly	Ala	Pro	Tyr	Asn	Leu	260	265	270	
Asn	Asp	His	Thr	His	Asp	Phe	Ser	Lys	Pro	Glu	Asp	Thr	Phe	Asp	Tyr	275	280	285	
Gln	Lys	Phe	Gly	Tyr	Ile	Tyr	Asp	Thr	Leu	Glu	Phe	Ala	Gly	Trp	Ser	290	295	300	
Ile	Arg	Gly	Ile	Asp	His	Ile	Val	Arg	Asn	Arg	Gln	Glu	His	Ser	Arg	305	310	315	320
Val	Phe	Ala	Gly	Phe	Leu	Leu	Glu	Gly	Phe	Gly	Thr	Ser	Ala	Thr	Val	325	330	335	
Asp	Phe	Gln	Val	Cys	Arg	Thr	Ala	Gly	Asp	Cys	Glu	Asp	Ala	Gly	Tyr	340	345	350	
Phe	Thr	Val	Leu	Gly	Gly	Glu	Lys	Glu	Met	Pro	Trp	Ala	Phe	Asp	Arg	355	360	365	

63

65

Asp Ala Met Arg Ala Val Met Ala Asp His Gly Pro Asn Gly Tyr Gln
35 40 45

Ala Ile Ala Ala Phe His Gly Asn Pro Pro Met Cys Pro Met Pro Asp
50 55 60

Gly Lys Asn Tyr Ser Cys Cys Thr His Gly Met Ala Thr Phe Pro His
65 70 75 80

Trp His Arg Leu Tyr Thr Lys Gln Met Glu Asp Ala Leu Thr Ala His
85 90 95

Gly Ala Arg Val Gly Leu Pro Tyr Trp Asp Gly Thr Thr Ala Phe Thr
100 105 110

Ala Leu Pro Thr Phe Val Thr Asp Glu Glu Asp Asn Pro Phe His His
115 120 125

Gly His Ile Asp Tyr Leu Gly Val Asp Thr Thr Arg Ser Pro Arg Asp
130 135 140

Lys Leu Phe Asn Asp Pro Glu Arg Gly Ser Glu Ser Phe Phe Tyr Arg
145 150 155 160

Gln Val Leu Leu Ala Leu Glu Gln Thr Asp Phe Cys Gln Phe Glu Val
165 170 175

Gln Phe Glu Ile Thr His Asn Ala Ile His Ser Trp Thr Gly Gly Leu
180 185 190

Thr Pro Tyr Gly Met Ser Thr Leu Glu Tyr Thr Thr Tyr Asp Pro Leu
195 200 205

Phe Trp Leu His His Ala Asn Thr Asp Arg Ile Trp Ala Ile Trp Gln
210 215 220

Ala Leu Gln Glu Tyr Arg Gly Leu Pro Tyr Asp His Ala Asn Cys Glu
225 230 235 240

Ile

<210> 73

<211> 98

<212> PRT

<213> Megathura crenulata

<400> 73

Lys His His Glu Lys His His Glu Asp His His Glu Asp Ile Leu Val
1 5 10 15

Arg Lys Asn Ile His Ser Leu Ser His His Glu Ala Glu Glu Leu Arg
20 25 30

Asp Ala Leu Tyr Lys Leu Gln Asn Asp Glu Ser His Gly Gly Tyr Glu
35 40 45

<400> 74															
Gly 1	Leu	Pro	Tyr	Trp 5	Asp	Trp	Thr	Met	Pro 10	Met	Ser	His	Leu	Pro 15	Glu
Leu	Ala	Thr	Ser 20	Glu	Thr	Tyr	Leu	Asp 25	Pro	Val	Thr	Gly	Glu 30	Thr	Lys
Asn	Asn	Pro 35	Phe	His	His	Ala	Gln 40	Val	Ala	Phe	Glu	Asn 45	Gly	Val	Thr
Ser	Arg 50	Asn	Pro	Asp	Ala	Lys 55	Leu	Phe	Met	Lys	Pro 60	Thr	Tyr	Gly	Asp
His 65	Thr	Tyr	Leu	Phe	Asp 70	Ser	Met	Ile	Tyr	Ala 75	Phe	Glu	Gln	Glu	Asp 80
Phe	Cys	Asp	Phe	Glu 85	Val	Gln	Tyr	Glu	Leu 90	Thr	His	Asn	Ala	Ile 95	His
Ala	Trp	Val	Gly 100	Gly	Ser	Glu	Lys	Tyr	Ser	Met	Ser	Ser	Leu 110	His	Tyr
Thr	Ala	Phe 115	Asp	Pro	Ile	Phe	Tyr	Leu	His	His	Ser	Asn 125	Val	Asp	Arg
Leu 130	Trp	Ala	Ile	Trp	Gln	Ala 135	Leu	Gln	Ile	Arg	Arg	Gly	Lys	Ser	Tyr
Lys 145	Ala	His	Cys	Ala	Ser 150	Ser	Gln	Glu	Arg	Glu 155	Pro	Leu	Lys	Pro	Phe 160
Ala	Phe	Ser	Ser	Pro 165	Leu	Asn	Asn	Asn	Glu 170	Lys	Thr	Tyr	His	Asn 175	Ser
Val	Pro	Thr	Asn 180	Val	Tyr	Asp	Tyr	Val	Gly	Val	Leu	His	Tyr 190	Arg	Tyr

<213> Megathura crenulata

<400> 76

Gly	Ser	His	Gln	Ala	Asp	Glu	Tyr	Arg	Glu	Ala	Val	Thr	Ser	Ala	Ser
1				5					10					15	
His	Ile	Arg	Lys	Asn	Ile	Arg	Asp	Leu	Ser	Glu	Gly	Glu	Ile	Glu	Ser
			20					25					30		
Ile	Arg	Ser	Ala	Phe	Leu	Gln	Ile	Gln	Lys	Glu	Gly	Ile	Tyr	Glu	Asn
		35					40					45			
Ile	Ala	Lys	Phe	His	Gly	Lys	Pro	Gly	Leu	Cys	Glu	His	Asp	Gly	His
	50					55					60				
Pro	Val	Ala	Cys	Cys	Val	His	Gly	Met	Pro	Thr	Phe	Pro	His	Trp	His
65					70					75					80
Arg	Leu	Tyr	Val	Leu	Gln	Val	Glu	Asn	Ala	Leu	Leu	Glu	Arg	Gly	Ser
				85					90					95	
Ala	Val	Ala	Val	Pro	Tyr	Trp	Asp	Trp	Thr	Glu	Lys	Ala	Asp	Ser	Leu
			100					105					110		
Pro	Ser	Leu	Ile	Asn	Asp	Ala	Thr	Tyr	Phe	Asn	Ser	Arg	Ser	Gln	Thr
		115					120					125			
Phe	Asp	Pro	Asn	Pro	Phe	Phe	Arg	Gly	His	Ile	Ala	Phe	Glu	Asn	Ala
	130					135					140				
Val	Thr	Ser	Arg	Asp	Pro	Gln	Pro	Glu	Leu	Trp	Asp	Asn	Lys	Asp	Phe
145					150					155					160
Tyr	Glu	Asn	Val	Met	Leu	Ala	Leu	Glu	Gln	Asp	Asn	Phe	Cys	Asp	Phe
				165					170					175	
Glu	Ile	Gln	Leu	Glu	Leu	Ile	His	Asn	Ala	Leu	His	Ser	Arg	Leu	Gly
			180					185						190	
Gly	Arg	Ala	Lys	Tyr	Ser	Leu	Ser	Ser	Leu	Asp	Tyr	Thr	Ala	Phe	Asp
		195					200					205			
Pro	Val	Phe	Phe	Leu	His	His	Ala	Asn	Val	Asp	Arg	Ile	Trp	Ala	Ile
	210					215					220				
Trp	Gln	Asp	Leu	Gln	Arg	Tyr	Arg	Lys	Lys	Pro	Tyr	Asn	Glu	Ala	Asp
225					230					235					240
Cys	Ala	Val	Asn	Glu	Met	Arg	Lys	Pro	Leu	Gln	Pro	Phe	Asn	Asn	Pro
				245					250					255	
Glu	Leu	Asn	Ser	Asp	Ser	Met	Thr	Leu	Lys	His	Asn	Leu	Pro	Gln	Asp
			260					265					270		
Ser	Phe	Asp	Tyr	Gln	Asn	Arg	Phe	Arg	Tyr	Gln	Tyr	Asp	Asn	Leu	Gln
		275					280					285			

70


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<210> 78
<211> 417
<212> PRT
<213> Megathura crenulata
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<400> 78

His Gly Ile Asn Val Arg His Val Gly Arg Asn Arg Ile Arg Met Glu
1 5 10 15

Leu Ser Glu Leu Thr Glu Arg Asp Leu Ala Ser Leu Lys Ser Ala Met
20 25 30

Arg Ser Leu Gln Ala Asp Asp Gly Val Asn Gly Tyr Gln Ala Ile Ala
35 40 45

Ser Phe His Gly Leu Pro Ala Ser Cys His Asp Asp Glu Gly His Glu
50 55 60

Ile Ala Cys Cys Ile His Gly Met Pro Val Phe Pro His Trp His Arg
65 70 75 80

Leu Tyr Thr Leu Gln Met Asp Met Ala Leu Leu Ser His Gly Ser Ala
85 90 95

Val	Ala	Ile	Pro	Tyr	Trp	Asp	Trp	Thr	Lys	Pro	Ile	Ser	Lys	Leu	Pro
			100					105					110		

Asp Leu Phe Thr Ser Pro Glu Tyr Tyr Asp Pro Trp Arg Asp Ala Val
115 120 125

Val Asn Asn Pro Phe Ala Lys Gly Tyr Ile Lys Ser Glu Asp Ala Tyr
130 135 140

Thr Val Arg Asp Pro Gln Asp Ile Leu Tyr His Leu Gln Asp Glu Thr
145 150 155 160

Gly Thr Ser Val Leu Leu Asp Gln Thr Leu Leu Ala Leu Glu Gln Thr
165 170 175

Asp Phe Cys Asp Phe Glu Val Gln Phe Glu Val Val His Asn Ala Ile
180 185 190

His Tyr Leu Val Gly Gly Arg Gln Val Tyr Ala Leu Ser Ser Gln His
195 200 205

Tyr Ala Ser Tyr Asp Pro Ala Phe Phe Ile His His Ser Phe Val Asp
210 215 220

Lys Ile Trp Ala Val Trp Gln Ala Leu Gln Lys Lys Arg Lys Arg Pro
225 230 235 240

Tyr His Lys Ala Asp Cys Ala Leu Asn Met Met Thr Lys Pro Met Arg
245 250 255

Pro Phe Ala His Asp Phe Asn His Asn Gly Phe Thr Lys Met His Ala
260 265 270

Asp	His	Ile	Ala	Gly	Ser	Gly	Val	Arg	Lys	Asp	Val	Thr	Ser	Leu	Thr
1				5					10					15	
Ala	Ser	Glu	Ile	Glu	Asn	Leu	Arg	His	Ala	Leu	Gln	Ser	Val	Met	Asp
			20					25					30		
Asp	Asp	Gly	Pro	Asn	Gly	Phe	Gln	Ala	Ile	Ala	Ala	Tyr	His	Gly	Ser
		35					40					45			
Pro	Pro	Met	Cys	His	Met	Xaa	Asp	Gly	Arg	Asp	Val	Ala	Cys	Cys	Thr
	50					55					60				
His	Gly	Met	Ala	Ser	Phe	Pro	His	Trp	His	Arg	Leu	Phe	Val	Lys	Gln
65					70					75					80
Met	Glu	Asp	Ala	Leu	Ala	Ala	His	Gly	Ala	His	Ile	Gly	Ile	Pro	Tyr
				85					90					95	
Trp	Asp	Trp	Thr	Ser	Ala	Phe	Ser	His	Leu	Pro	Ala	Leu	Val	Thr	Asp
			100					105					110		

<210> 80
 <211> 1266
 <212> DNA
 <213> *Haliotis tuberculata*

<400> 80
 cttgttcagt ttctactcgt cgcccttgtg gtgggggctg gagcagacaa cgtcgtcaga 60
 aaggacgtga gtcacctcac ggatgacgag gtgcaagctc tccacggcgc cctccatgac 120
 gtcactgcat ctacagggcc tctgagtttc gaagacataa catcttacca tgccgcacca 180
 gcgctcgtgtg actacaaggg acggaagatc gcctgctgtg tccacggtat gccagtttc 240
 cccttctggc acagggcata tgtcgtccaa gccgagcggg cactgttgctc caaacggaag 300
 actgtcggaa tgccttactg ggactggacg caaacgctga ctacttacc atctcttgtg 360
 actgaaccca totacattga cagtaaagggt ggaaaggctc aaaccaacta ctggtaccgc 420
 ggcgagatag cgttcatcaa taagaagact gcgcgagctg tagatgatcg cctattcgag 480
 aagggtggagc ctggtcacta cacacatctt atggagactg tctcgcacgc tctcgaacag 540
 gacgaattct gtaaatttga aatccagttc gagttggctc ataatgctat ccattacttg 600
 gttggcggta aatttgaata ttcaatgtca aacttggaa acacctccta cgaccccatc 660
 ttcttctctc accactccaa cgttgaccgc ctcttcgcca tctggcagcg tcttcaggaa 720
 ctgcgaggaa agaatcccaa tgcaatggac tgtgcacatg aactcgctca ccagcaactc 780
 caacccttca acagggacag caatccagtc cagctcacia aggaccactc gacacctgct 840
 gacctctttg attacaaaca acttggtatc agctacgaca gcttaaacct gaatggaatg 900
 acgccagaac agctgaaaac agaactagac gaacgccact ccaaagaacg tgcgtttgca 960
 agcttccgac tcagtggctt tgggggttct gccaacgttg ttgtctatgc atgtgtccct 1020
 gatgatgatc cacgcagtga tgactactgc gagaaagcag gcgacttctt cattcttggg 1080
 ggtcaaagcg aaatgccgtg gagattctac agacccttct tctatgatgt aactgaagcg 1140
 gtacatcacc ttggagtccc gctaagtggc cactactatg tgaaaacaga actcttcagc 1200
 gtgaatggca cagcactttc acctgatctt ctctctcaac caactgttgc ctaccgacct 1260
 gggaaa 1266

<210> 81
 <211> 1257
 <212> DNA
 <213> *Haliotis tuberculata*

<400> 81
 ggtcaccttg acccacctgt gcatcatcgc cacgatgacg atcttattgt tcgaaaaaat 60
 atagatcatt tgactcgtga agaggaatac gagctaagga tggctctgga gagattccag 120
 gccgacacat ccgttgatgg gtaccaggct acagtagagt accatggcct tctgtctcgt 180
 tgteccacgac cagatgcaaa agtcaggctt gcctgttgta tgcattggat gccatccttc 240
 cctcactggc accggctggt cggtacccag gtggaagatg ctcttgtagc gcgtggatcg 300
 cctatcggtg ttctttattg ggactggaca aaacctatga ctacacctcc agacttggca 360
 tcaaatgaga cgtacgtaga cccgtatgga catacacatc ataattccatt ctccaatgca 420
 aatatactct ttgaggaggg acaccatcac acgagcagga tgatagattc gaaactgttt 480
 gccccagtcg cttttgggga gcattcccat ctgtttgatg gaatcctgta cgcatttgag 540
 cagggaagatt tctgcgactt tgagattcag tttgagttag tccataatct tattcatgag 600
 tggataggcg gttccgaaga ttactccatg gccaccctgc attacacagc ctttgacccc 660
 attttctacc ttcatcttcc caatgtcgat cgtctatggg caatctggca agctcttcaa 720
 atcaggagac acaagccata tcaagcccac tgtgcacagt ctgtggaaca gttgccaatg 780
 aagccatttg ctttcccatc acctcttaac aacaacgaga agacacatag tcattcagtc 840
 ccgactgaca tttatgacta cgagggaagt ctgcactaca gctacgatga tctaactgtt 900
 ggtgggatga accttgaaga aatagaagaa gctatacatc tcagacaaca gcatgaacga 960
 gtcttcgagg gatttctcct tgcgtggaata ggaacatctg cacttggtga cattttcata 1020
 aataaacggg ggaaccaacc actcaaagct ggagatattg ccattcttgg tgggtgccaag 1080
 gaaatgcctt gggcgtttga ccgcttgatg aaggctcgaa taactgactc attgaagaca 1140
 ctttctctcg atgtcgatgg agattatgaa gtcactttta aaattcatga tatgcacgga 1200
 aacgctcttg atacggacct gattccacac gcagcagttg tttctgagcc agctcac 1257

<210> 82
<211> 1242
<212> DNA
<213> *Haliotis tuberculata*

<400> 82
cctacctttg aggatgaaaa gcacagctta cgaatcagaa aaaatgtcga cagcttgact 60
cctgaagaaa caaatgaact gcgtaaagcc ctggagcttc ttgaaaatga tcatactgca 120
ggtggattca atcagcttgg cgccctccat ggagagccta aatgggtgcc taatcctgaa 180
gcggagcaca aggttgcatt ctgtgttcat ggcatggctg tttccctca ttggcacagg 240
cttcttgctc tccaggcgga gaatgctctt agaaagcatg ggtacagtgg tgctctacca 300
tactgggatt ggactcgccc cctttcccaa ctccctgac tggttagtca tgagcagtat 360
acagatcctt ccgaccatca cgtgaagcat aaccctgtgt tcaatggcca catcgatata 420
gtaaatcagg ataccaccag aagcgtacgg gaggatcttt atcaacaacc tgaatttgga 480
catttcacgg atattgtctc acaagtcctc ttagcattag aacaagatga cttctgttcg 540
tttgaagtgc agtatgagat ttcccataat tttatccatg cacttgtagg aggaaccgac 600
gcttatggca tggcatcgct gagatataca gcatacgatc caatcttttt cttgcatcat 660
tcaaacaccg acaggatctg ggctatattg caatccctgc aaaaatacag aggcaaaccg 720
tacaacactg ccaactgcgc catagaatct atgagaaggc ccctgcaacc atttggacta 780
agcagtgcc aataacctga cagaatcacc agagagcatg ctatcccgtt tgatgtcttc 840
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gacctgttcc acactgcaaa tgtggtacat gattccggca ca 1242

<210> 83
<211> 1239
<212> DNA
<213> *Haliotis tuberculata*

<400> 83
ggcaccctgt atcgtgataa ctacgttgaa gaagttactg gggccagtca tatcaggaag 60
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caggacgacg gaacatatga atctattgcc cagtaccatg gcaaaccagg caaatgtcaa 180
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<210> 86
 <211> 1209
 <212> DNA
 <213> *Haliotis tuberculata*

<400> 86
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 aacaccttga ctaaggctga gaccgacaac ctgagggagg cgctgtgggg tgtcatggca 120
 gaccacggtc ccaatggctt tcaagctatt gctgctttcc atggaaaacc agcttttgtgt 180
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 ggctgacct actgggactg gactgctgcc ttcaccacac tgccaacact ggtcacccgac 360
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 aaggtgatga agcagctaca cctgaggcat gactctgact ttaccttcag ggtgaagatt 1140
 gtcggcaccg acgaccacga gcttccttca gacagtgtca aagcaccaac tattgaattt 1200
 gaaccgggc 1209

<210> 87
 <211> 1536
 <212> DNA
 <213> *Haliotis tuberculata*

<400> 87
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 tacaagctcc agaatgacga cagtaaaggg ggctttgagg ccatagctgg ctatcacggg 180
 tatectaata tgtgtccaga aagaggtacc gacaagtatc cctgctgtgt ccacggaatg 240
 cccgtgttcc cccactggca ccgcctgcat accattcaga tggagagagc tctgaaaaac 300
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79

gctatggcta aatgcacgtg tccccctttc tttaccacg gctttgaact ggacaaagtc 1440
tacagcgctg atcacggaga ctactacatt gctgcaggta cccacgcgtt gtgtgagcag 1500
aacctcaggc tccacatcca cgtggaacac gagtag 1536

<210> 88

<211> 591

<212> DNA

<213> *Haliotis tuberculata*

<400> 88

ggtcttccgt actgggactg gacgcagcat ctgactcaac tcccagatct ggtgtcagac 60
cccttgtttg tgcacccgga aggaggaaag gcccatgaca acgcatggta tegtggaaac 120
atcaagtttg agaataagaa gactgcaaga gctggtgacg atcgctttt cgagaagggt 180
ggaccaggag agaatacccg actcttttgaa ggaattctcg atgctcttga acaggatgaa 240
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ggaaaggacc ccaacacgcg cgactgcgca cacaacctca tccatgagcc catggaaccg 480
ttccgtcggc atgagcccat ggaaccgttc cgtcgggact cgaacctct tgacctcacc 540
agggaaaact ccaaaccaat tgacagcttt gattatgccc accttggtta c 591

<210> 89

<211> 1245

<212> DNA

<213> *Haliotis tuberculata*

<400> 89

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acatccgttg atgggtacca ggctacggtt gagtatcacg gcttacctgc tgcagtcca 180
ttccccgagg ccacaaatag gtccgctgt tgcacccacg gcatggcgac attccctcat 240
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gccacctata gagatcccat cagcggggac agcagacaca accccttcca cgatgttgaa 420
gttgcccttg aaaatggacg tacagaacgt caccagata gtagattgtt tgaacaacct 480
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cttcgtcact ccaacactga ccggctcttg gcaatttggc aagcgttgca gatacgaaga 720
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gctgatgatg ttttcagcat ctctgttaaa gtaactgatg ttgatggcag tgagctgtcc 1200
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<210> 90

<211> 1251

<212> DNA

<213> *Haliotis assimilis*

<400> 90

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cccaggagaaa ttaattctct gaggcgggca atggcagacc ttcaatcaga caaaaccgcc 120

80

ggtggattcc	agcaaattgc	tgcttttccac	ggggaaccca	aatgggtgcc	aagtccegat	180
gctgagaaga	agttctcctg	ctgtgtccat	ggaatggctg	tcttccctca	ctggcacaga	240
ctcctgaccg	tgcaaggcga	gaatgccctg	agaaagcatg	gatgtctcgg	agctctcccc	300
tactgggact	ggactcggcc	cctgtctcac	ctacctgatt	tggttttggg	aagtagcaga	360
actacaccga	tgccatattc	caccgtggaa	gcccgaacc	cctggtacag	cggccatatt	420
gatacagttg	gtgttgacac	aacaagaagc	gtccgtcaag	aactgtatga	agctcctgga	480
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aaaccttaca	attccgcca	ctgcgccatt	gcttctatga	gaaaaccctt	acaacccttt	780
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<210> 91

<211> 1242

<212> DNA

<213> *Haliotis tuberculata*

<400> 91

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cagaacgacg	gagtctatga	gaatattgcc	aagttccacg	gcaagcctgg	gttgtgtgat	180
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ccatactggg	actggactga	aacattttaca	gagctgccat	ctttgattgc	tgaggctacc	360
tattttcaatt	cccgtaacaa	aacgtttgac	cctaatectt	tcttcagagg	taaaatcagt	420
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<210> 92

<211> 1257

<212> DNA

<213> *Haliotis tuberculata*

<400> 92

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cattcacctg	acgggttcca	agccattgcc	tctttccatg	ctctgccacc	actctgcctt	180

81

tcaccatctg	cagctcaccg	ttatgcttgc	tgtgtccacg	gcattggctac	atttccccag	240
tggcacagat	tgtacactgt	acagttccag	gatgcactga	ggagacatgg	agctacggta	300
ggtgtaccgt	attgggattg	gctgcgaccg	cagtctcacc	taccagagct	tgtcaccatg	360
gagacatacc	atgatatttg	gagtaacaga	gatttcccca	atcctttcta	ccaagccaat	420
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<210> 93

<211> 1248

<212> DNA

<213> *Haliotis tuberculata*

<400> 93

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cccaacggat	accaggtctt	tgcagccttc	catgggctac	cagcaggctg	ccatgatagc	180
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<210> 94

<211> 1206

<212> DNA

<213> *Haliotis tuberculata*

<400> 94

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82

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<213> *Haliotis tuberculata*

<400> 95

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<212> DNA

<213> *Megathura crenulata*

<400> 96

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85

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<212> DNA

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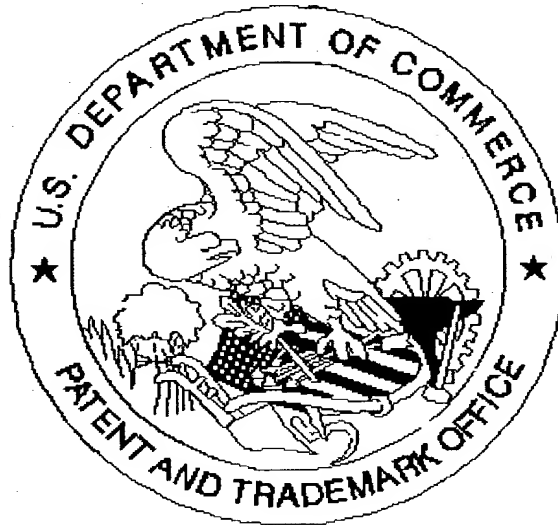
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